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THE  
GALL STONE DISEASE

A CLINICAL-STATISTICAL STUDY

BY

ERNST EHNMARK

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FROM THE SURGICAL CLINIC OF THE UNIVERSITY OF UPPSALA  
(CHIEF: PROFESSOR GUNNAR NYSTRÖM)

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MED. LIC., NORRL.

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ELANDERS BOKTRYCKERI AKTIEBOLAG



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## PREFACE.

The present investigation was based on a material of 1061 cases of gall stone disease, of which 563 were operated on, and 498 were not operated on, during the first stay in the hospital. The object was to obtain an idea of the risk factors in gall stone disease. The author has tried to establish the risk applying to an attack, attended, or not attended, by operation, and also, by re-examination, tried to obtain a survey of the risk involved in different forms of the disease and the mortality during the subsequent course of the disease. It was of special interest to try to examine different indications for surgical treatment of acute cholecystitis, as they have to a certain extent been modified during the period covered by the material. In the treatment of the material the author tried to arrive at a more satisfactory statistical analysis. Previous investigations are in many ways imperfect, not only from a methodical point of view. The data on the materials given are often incomplete. Mostly, information is only given on cases operated on. Further, there exists no satisfactory survey of the risk factors in gall stone disease from the point of view of the population, either with reference to the risk of developing gall stone, the risk of being taken ill, or the risk of dying. The present paper aims at filling up, as far as possible, these gaps in the literature.

In presenting the result of my investigations it is my pleasant duty to express my gratitude to Professor GUNNAR NYSTRÖM for the valuable help and great encouragement he has given me in the course of my work, and for his courtesy in giving me the opportunity to study cases of gall stone disease and collect material during the years in which I was attached to his clinic. This investigation was rendered possible only because the diary material from the surgical department of the Academical Hospital was kindly placed at my disposal.

In the treatment of the material I have obtained valuable advice and helpful suggestions from Professor GUNNAR DAHLBERG, head of



the State Institute of Human Genetics and Race Biology in Uppsala, for which I beg to tender my sincere thanks. Further, I wish to express my appreciation of his courtesy in allowing me to work in his Institute during several months, while making the statistical analysis of the material. I am also very grateful for the assistance given me by the staff of the Institute in carrying out the statistical calculations. I want to thank especially Mr. E. LANDER.

I am also indebted to Professor G. BERGMARK, who kindly allowed me to make use of the diary material from the medical department of the Academical Hospital, to Professor R. FÄHRÆUS for his courtesy in placing at my disposal autopsy material from the Pathological Institution in Uppsala, and Mr. E. J. HÖJER, temporary director-in-chief of the Central Statistical Bureau in Stockholm, who has kindly placed at my disposal data from the official statistics.

In preparing the survey of the early literature I have had valuable assistance from Professor E. NACHMANSSON in Gothenburg and Doctor E. WALLER, Lidköping.

I further beg to present my thanks to Professor SVEN JOHANSSON in Gothenburg for much good advice during the course of the work.

I should also like to express my appreciation of the assistance given me by the Library Authorities in Uppsala and Gothenburg.

The translation of my paper was carried out by Miss A. LIEDHOLM, F. L., to whom I beg to present my best thanks.

Finally, my thanks are due to Regnell's fund at the Medical Faculty in Uppsala for contributions towards the expenses entailed in my work.

The primary material is not presented in this paper. In the University Library in Uppsala I have deposited a specification of diary numbers relating to the clinical material, and also the answers to the questionnaires on which the re-examinations were based.

Uppsala, April 1939.

*Ernst Ehnmark.*

## INTRODUCTION.

Gall stones occur at all ages, both in men and women. There exists a comprehensive literature on the cause of the formation of gall stones. Many authors are of the opinion that infection of the gall bladder causes formation of stones; it is further thought that hindrance to the emptying of the gall bladder favours this formation, and, finally, it is assumed that disturbances in the metabolism exercise a certain influence on the formation of stones.

Examinations of autopsy cases have shown that gall stones are present more frequently, the older are the cases examined, both in men and women. If the examined autopsy materials are representative of the population to which they belong, we have reason to assume a frequency of gall stones in the population which increases with increasing age. This being so, a risk of gall stone formation must be present during the whole lifetime, a risk, the magnitude of which we do not know.

By gall stone disease in an extended sense we mean the clinical pictures of disease which may arise in the presence of gall stones in the gall bladder and biliary ducts. The character of the clinical symptoms may vary. Sometimes attacks of pains are most prominent. In certain cases, these attacks are combined with symptoms of infection which in their turn may also dominate the clinical picture. Further, the symptoms may be more acute, or more chronic, in character, which brings out differences in the general picture of the disease. As is known, clinical pictures of a similar type also occur in diseases of different genesis, for instance infection only of the gall bladder, or in tumour of the gall bladder. The differential-diagnostic problems are not always easy to solve. It is not difficult, however, to remove the cases of tumour. Cases of gall stone disease without stones, that is to say cases which do not clinically differ from the picture obtained in cases of gall stone, but in which stones are absent, on the other hand present difficulties. We shall briefly discuss this problem below.

The part played by gall stones in causing gall stone disease is not elucidated. We know that only part of the gall stone carriers develop gall stone disease. Many authors are of the opinion that infection of the gall bladder or biliary ducts is the primary stage not only in the formation of gall stones but also in the development of gall stone disease. In support of this view it has been stated that more or less pronounced inflammatory changes of the gall bladder may be demonstrated in many cases, and that, further, inflammation of the gall bladder may appear without the latter containing any stones (non-calculous cholecystitis). These latter cases, however, are not very numerous. During a period of 14 years, covered by our clinical material, 268 cases of acute cholecystitis were operated on. In 11 out of the cases, the gall bladder contained no stone (that is to say in 4.1 per cent of the cases operated on). During the same period, 87 cases of chronic cholecystitis were operated on. In one of these cases the gall bladder contained no stone (i. e. in 1.2 per cent of the cases operated on). The relation between non-calculous cholecystitis and calculous cholecystitis is of the same order of magnitude in many other materials published. As, in the majority of cases of »gall stone disease», we find stones in the gall bladder, there must exist an obvious relation between gall stone and gall stone disease. This statement does not mean that we take up a definite position in reference to the question as to the extent to which infection, even of a very mild nature (free from symptoms), is the primary factor, and the extent to which infection of a sometimes very severe type may be exclusively a secondary factor. The comprehensive literature on these problems cannot be reviewed here. We have only wished to call attention to well-known points of view in order to create a background to our terminology and formulation of the problems. The question as to the extent to which infection of the gall bladder is decisive to the development of gall stone and gall stone disease, in some measure falls beyond the scope of the present investigation, although we shall touch upon this problem. In the following discussion we use the term »gall stone disease» only of the cases in which, in addition to the morbid symptoms, stone in the gall bladder or biliary ducts is present, in so far as we are concerned with autopsy material or operations. The material included in our investigation in which the diagnosis was made exclusively on the basis of clinical symptoms, however, doubtless comprises a small



number of cases without stone. The figures presented above, however, show that such cases hardly have a high frequency; consequently we have no reason to assume that they will essentially influence the figures we have obtained.

By observations of clinical materials, attempts have been made to arrive at an idea of the frequency of the gall stone disease. The figures obtained, however, only refer to the relative number of cases in different age groups in a material of gall stone patients. The question of the frequency of the gall stone disease from the point of view of the population has not been treated, that is to say the number of patients belonging to different age groups and sexes has not been related to the population from which the material was collected. If this is done, we ought to obtain an idea also of the risk of developing gall stone disease which, as seen from the point of view of the population, exists for men and women in different age groups.

On the basis of clinical materials, the risk of dying of gall stone disease has also been treated; it has been found that this risk increases with age and that the risk varies according to the forms in which the disease appears. The risk of dying of gall stone disease from the point of view of the population has not been determined, however.

There exists an extremely rich literature on the symptomatology and prognosis of the gall stone disease. However, in most cases the authors only deal with series of cases operated on, or else with series of patients not operated on. As a rule, only a certain form of the disease is treated, for instance acute cholecystitis, usually on the basis of a material comprising only patients operated on, or only patients not operated on. So far, there does not exist a comprehensive material of gall stone disease in its various forms, comprising patients treated both operatively and conservatively. Such a material no doubt should be capable of giving valuable information on the immediate prognosis of the disease, its tendency to relapse, and so forth, information which cannot be obtained on the basis of materials as yet published.

The object of the present investigation is to try in some measure to fill up these gaps in our knowledge of gall stone and gall stone disease.

After a survey of the literature in chapter 1, an account of the materials is given in chapter 2, and of statistical methods employed in chapter 3. In chapter 4 gall stone and gall stone disease are treated

from a demographic point of view. The clinical material is dealt with in chapters 5 and 6. In chapter 5 are treated the cases not operated on during their first stay in hospital, particularly with regard to the results of primary treatment and the risk of relapse; in chapter 6, the cases operated on are dealt with in the same manner. In chapter 7 is discussed the risk run by those who contract gall stone disease of falling ill with different forms of the disease, of relapsing, and of dying.

## CHAPTER I.

### Review of the Literature.

ANTONIO BENIVIENI (1440—1502) was the first to describe gall stone and gall stone disease and to relate them to each other. Gall stone, however, is said to have been mentioned even earlier, by GENTILIS DA FOLIGNO († 1348). According to MARCELLUS DONATUS, who in 1586 published »De medica historia mirabili», DA FOLIGNO in a post-mortem examination of a woman had found a greenish-looking stone in the duct of the gall bladder, at its mouth.<sup>1)</sup> According to another source<sup>2)</sup> this finding was made by DA FOLIGNO in the year 1341 in the first post-mortem examination that was made at the university of Padua. In the works by DA FOLIGNO which are still extant, there are no data relating to a finding of gall stone, however (MULEUR).

Gall stone and gall stone disease are nowadays comparatively common complaints. It is probable that they existed long before the time implied by the data quoted above. Gall stone existed in ancient times: gall stones were found in the gall bladder of a mummy (a priestess of Amenem of the XXI Dynasty.)<sup>3)</sup> No data, however, are found on gall stone or gall stone disease in the early literature, either in the works of classical medicine or in the works which were published during the first 1500 years of our era.<sup>1)</sup> Certain case histories in the HIPPOCRATIC works, as in the works by GALEN, might be interpreted, it is true, as if they referred to patients suffering from biliary colic. Such an interpretation, however, is mere guesswork.

Before autopsies on human beings had begun to be made (in the beginning of the 14th century A. D.), people had very vague notions

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<sup>1)</sup> See MULEUR.

<sup>2)</sup> NEUBURGER and PAGEL: Handbuch der Geschichte der Medizin II, p. 200.

<sup>3)</sup> The mummy, which was taken from Deir-el-Bahan, Thebes, was in 1909 given by Sir Crafton Elliot-Smith to the Royal College of Surgeons Collection in London. See GORDON-TAYLOR.



of anatomy, and it was no doubt impossible to diagnose the gall stone disease exclusively on the basis of clinical symptoms. Abscesses in the liver were comparatively well known; such abscesses were, and still are, common in the countries round the Mediterranean. It is not impossible that cases of acute cholecystitis, if they occurred, were diagnosed and treated as such abscesses. Now and then, an inflamed gall bladder perforates in an outward direction, and stones escape through the fistula developed in this manner. If such cases had been observed, it would have been possible to diagnose gall stone disease. Such cases, however, are rare. COURVOISIER, from the literature available in 1890, was only able to collect 196 cases, 13 of which dated from the time before the year 1700, and 34 before the year 1800.

We return to ANTONIO BENIVIENTI. In his posthumous work »De abditis nonnullis ac mirandis morborum et sanationum causis«, which was published in 1507, he inter alia gives two case histories referring to women who had been taken ill with severe pains in the upper portion of the abdomen and later died from their disease. In the post-mortem examination stones were found in the gall bladder. BENIVIENTI inferred that the gall stones had caused the disease.

When, in the beginning of the 16th century, attention had been drawn to gall stone and gall stone disease, a fairly extensive literature was before long written on this subject. RHODIGINIS (1516) and LANGIUS DE LEMBERG (1554) described gall stone. REALDUS COLUMBUS, in the post-mortem examination of Ignatius Loyola, found numerous stones both in the ureters, the bladder, the intestines and in the gall bladder. VESALIUS (1561) described stone both in the gall bladder and in the duct leading from the liver to the duodenum. FERNEL (1554) observed that in jaundice feces were white, the urine dark, and that stones were sometimes passed with the feces. PARACELUSUS (1498—1546) held that stone formation had partly constitutional, partly local, causes and that, in certain cases, it might be hereditary. The first detailed description of gall stone was given by KENTMANN in the year 1565. COITER, who in 1573 described a case of jaundice, in the autopsy found a stone which obturated the common bile duct and supposed that this was the cause of the jaundice. — The observations on gall stone and gall stone disease, which were made during the 16th century, were mostly looked upon as a curiosity, however.

During the 17th century both gall stone and gall stone disease became the object of a much greater interest, and discussions were held on the cause of gall stone formation (HULDENREICH, BONNET, and others).

GLISSON, whose important work »*Anatomia hepatis*» was published in 1654, examined liver and biliary ducts in cattle and found stone both in gall bladder and biliary ducts. He observed that gall stones were sometimes passed with feces in man, and supposed that stone passed from the gall bladder through the biliary ducts to the intestines, assuming that the biliary ducts were contractile. He was of the opinion, however, that the pains were not caused by such a passage of stone. (He suffered from attacks of biliary colic himself, which he describes very vividly: pains radiating up to the right collar bone, vomitings, and at times jaundice). WEPFER (1658) showed that jaundice was sometimes present in cases of stone in the common bile duct or the hepatic duct, but not in cases where stone was only present in the gall bladder and the biliary ducts were free.

The first known operations performed in order to remove gall stone, are related by STALPART VAN DER WIELL (1666): a certain Doctor LIEBERGER from Hague is said to have opened an abscess of the liver in which he found a stone the size of a dove's egg.<sup>1)</sup> In 1670, THILESIIUS described a case in which the patient had an abscess in the region of the liver which opened spontaneously. From the fistula created in this manner, small stones were now and then passed during a time of 9 years. So long as the fistula remained open, the patient was in good health; if it closed, the patient developed jaundice.

Towards the end of the 17th century it was fairly well known that jaundice might develop by the biliary duct being closed by a stone. It was further known that gall stone could be found in the feces after typical attacks of biliary colic. The gall stone disease aroused comparatively little interest, however. The cause of gall stone formation, on the other hand, was much discussed, as also the cause of stone formation in other organs (kidney, bladder, etc.). The controversy was held between the two leading schools, the chemiatic and the physiatic.

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<sup>1)</sup> The frequently quoted statement that JOH. FABRICIUS had made a similar operation as early as 1618 is thought to be based on a misconception: the stone had probably been found in a post-mortem examination. Cf. ROTH.

The first attempts to remove the gall bladder in animals date from the 17th century. ZAMBECCARI in 1680 extirpated the gall bladder in a dog, after the cystic duct had been ligatured. The operation succeeded, and the dog showed no morbid symptoms during the post-operative period.

The 18th century inaugurates a new era in the history of the gall stone disease. The interest was more and more centred on the clinical picture of the gall stone disease (BIANCHI, VATER, VALLISNIERI, and others). Gall stones were examined with great interest. GIUDETTUS described two types of gall stones: black ones which sank in water and could only with difficulty be burnt; yellow stones which usually floated on water, were stratified and easily combustible.

In 1733, HOFFMANN wrote about the connection between gastric pains and gall stone. He pointed out that the gall bladder emptied itself only when it was compressed by the stomach being filled with food. A too long interval between meals might result in stagnation of the bile and formation of stone in the gall bladder. Women had gall stone more frequently than men, particularly in the menopause. He further mentioned that stones in the gall bladder did not cause discomforts except when, for some reason or other, the stones began to move and changed their position. Pain was caused by a stone entering the biliary duct. He had also observed cases in which stone was found in the gall bladder of persons who had never had attacks of pain.

TACCONI in 1740 described an operation for gall stone. The patient was a woman who had had numerous attacks of biliary colic and who had finally got into a prolonged feverish state and had a solid, slowly growing tumour in the region of the liver. The tumour was split until a cavity was reached in which 7 stones were found. At first bile flowed from the wound and another number of stones were passed. Gradually the patient recovered.

The year 1743 is a memorable year in the history of the gall stone disease. In this year JEAN LOUIS PETIT published his famous work: *»Remarque sur les Tumeurs formées par la bile retenue dans la vésicule du fiel, et qu'on a souvent prises pour des abcès au foye.»*

PETIT parallels the urinary bladder and the gall bladder as regards obstruction to the emptying of these organs. In both cases obstruction to the emptying might be caused in two ways. Either the excre-



tory duct of the organ is closed, most frequently by a stone, or the power of contraction of the organ is reduced or lost. PETIT had actually observed cases in which the palpable, distended gall bladder emptied on certain occasions, particularly when the patient occupied a horizontal position. Relating to the disappearance of the tumour of the gall bladder, the feces contained abundant amounts of bile. PETIT further points out that retention of bile in the gall bladder could be complicated by inflammation of the latter. Inflammation of the gall bladder ought to be treated operatively in suitable cases; it was, however, dangerous to open the gall bladder in the cases in which it did not adhere to the anterior wall of the abdomen. That this was the case might be assumed when the distended gall bladder was not freely movable in relation to the abdominal wall, and also if the skin over the gall bladder was flushed and inflamed. The operation was performed as follows. The gall bladder was punctured with a trocar and emptied. Then it was explored by probe, and possibly by the finger, and the stones were removed. PETIT, who was one of the best physicians of his time, uttered the sensible words: «Ce que j'en ai dit est suffisant pour modérer l'ardeur des jeunes gens qui veulent toujours couper; mais aussi ne faut-il pas qu'une timidité mal entendue leur fasse manquer l'occasion d'opérer.» It is worthy of notice that PETIT introduced the term «colique hépatique.»

PETIT's work gave the impulse to a more extensive surgical treatment of the gall bladder disease; many physicians objected, however, to the method of treatment suggested by him. SHARP (1750), MORAND (1757), and others operated on several cases. HALLER (1753) found that both gall bladder and common duct were provided with muscular tissue and by experiments on animals he was able to show that they were capable of contracting. He was of the opinion that stone did not cause pain if it was present in the gall bladder but only if it had got down to the cystic duct, and that, as a rule, operation ought not to be performed for the reason that it was very difficult to remove a stone in the cystic duct. SOEMMERING (1795), like BROMFIELD (1773), if possible avoided to operate on persons suffering from gall stone disease. BLOCH (1774) suggested that in the cases where the gall bladder did not adhere to the anterior abdominal wall, attempts should be made to cause a growing together of the gall bladder and the peritoneum of the anterior abdominal wall by

caustic agencies. RICHTER (1798) adopted this suggestion and proceeded in the following manner: he incised close to the peritoneum and then applied a caustic close to the latter. After a time, adhesions had developed, and the gall bladder could be opened without risk. In other cases he opened the gall bladder with a trocar and emptied it. After a couple of days, the fistula was dilated and the stones were removed. He further made attempts to remove stones from the common bile duct with the aid of a probe.

In 1767, HERLIN, L'ANGLAS and DUCHAINOIS performed experimental cholecystectomy and showed that the gall bladder could be removed without the test animals (dogs and cats) showing any morbid symptoms after the operation. They suggested that the same operation should be performed on human beings suffering from gall stone disease. Their work was subsequently forgotten, however, and does not seem to have exercised any influence on the treatment of gall stone disease.

We find a few additional communications of interest from the 18th century. VAN SWIETEN recommended (1753) the use of opium in attacks of biliary colic partly to alleviate the pain and partly in order to suppress the cramp in the biliary ducts. DURANDE showed (1774) that gall stone could be dissolved in a mixture of ether and turpentine. This resulted in attempts being made to cure gall stone disease by administering these substances to the patients.

In the first half of the 19th century there were not many fresh contributions to the treatment of gall stone disease. DELPECH (1816) was very cautious in the matter of operation. He incised only when he was able to feel a fluctuation in the gall bladder tumour. GOOD (1825) had unfavourable experiences of incision for cholecystitis: he had observed cases in which new stones were formed in the gall bladder. SEBASTIAN (1827), and later on FAUCONNEAU-DUFRESNE (1847), readopted RICHTER's method of trying to produce adhesions between the gall bladder and the peritoneum of the anterior abdominal wall by applying corrosive agents.

During the latter half of the 19th century, the treatment of the gall stone disease, as of so many other diseases, was wholly revolutionized. The new methods of operation which were then invented, had been proposed at an earlier date, although they had not then been duly considered. We have already mentioned ZAMBECCARI's experimental cholecystectomy and HERLIN, L'ANGLAS and DUCHAI-

NOIS's view, based on experiments on animals, to the effect that it ought to be possible to remove the gall bladder. In 1833, CARRÉ suggested that an operation should be carried out by making an incision into the gall bladder. If the latter proved to be adherent to the abdominal wall, it could be opened in the same séance. Otherwise, the operator had better wait a few days until adhesions had been formed, when the gall bladder should be opened. In 1859, THUDICUM made a similar suggestion: if the gall bladder was not adherent to the abdominal wall, it ought to be sewed on to the parietal peritoneum. After about 6 days had elapsed, it could be opened without risk of peritonitis. None of the proposals, however, were acted upon. It was BOBBS that in 1867 performed the first cholecystostomy by way of a free peritoneal cavity. He operated for an abdominal tumour which was considered to be an ovarian cyst but was in point of fact a strongly distended gall bladder. The latter was sewed on to the wound and opened.

To MARION SIMS, however, should be ascribed the priority of having performed cholecystostomy (in one séance) for diagnosed gall stone disease (1878). KOCHER in the same year also performed a cholecystostomy (in 2 séances), and KEEN made this operation in 1879. Before long, cholecystostomy became a method of operation comparatively often employed.

A modification of the method, so-called ideal cholecystotomy, in which the gall bladder, after stones had been removed, was sewed up and sunk into the abdominal cavity, was performed for the first time in 1883 by MEREDITH, and for the first time with satisfactory result by COURVOISIER in 1884.

In the cases where stone in the common bile duct obstructed the flow of bile to the intestines, attempts were made to remove the obstruction by probing from a cholecystostomy. PARKES (1885) and v. WINIWARTER (1888) described successful such operations.

In isolated cases it was possible to remove stone in the common bile duct by way of the dilated cystic duct (e. g. LANGE, 1886, CRÉDÉ 1886, LANGENBUCH, 1886). These methods, however, were seldom successful. KÜMMEL stated in 1890 that in the beginning of the eighties, »als gerade die Langenbuch'sche Cholecystectomy empfohlen war», he had opened the common bile duct and removed stone from it. COURVOISIER in 1890 worked out the same method without know-



ledge of his predecessor, and this method soon became the standard method in cases with stone in the common duct.

v. WINIWARTER in 1881 performed the first anastomosis between gall bladder and intestines in a case in which he could not remove an obstruction in the common bile duct.

Cholecystectomy, the operation which has been of the greatest importance to the surgery of the biliary tract, was performed for the first time on July 15th, 1882, by LANGENBUCH.

The history of gall stone and gall stone disease enters upon a new phase at the end of the 19th century, when more rational methods of treatment had been worked out. With the more widespread use of the new operative methods of treatment, it is the surgical treatment of gall stone disease that dominates the literature. Simultaneously with these, new possibilities, so far unknown, presented themselves of observing the changes which in the various forms of gall stone disease were to be found in gall bladder and biliary ducts. A result of this, and of the advances made by medical and physiological chemistry at the end of the 19th century, was that the so far rather speculative theories on the development of gall stone and on the relation between gall stone and gall stone disease were replaced by statements based on observations.

In the following pages we shall give a survey of the views on the development of gall stone and gall stone disease, and also give an account of different opinions relating to the treatment of the gall stone disease. The review does not claim to be in any way complete; the extremely rich literature on the subject renders this impossible.

#### *Gall stone and gall stone formation.*

The theories which in the early literature were advanced on gall stone formation, are an expression of the views held on stone formation generally, and mirror the conception of the development of morbid processes characteristic of different times. Only at the end of the 18th century was it observed that gall stones had certain specific chemical properties. POULLETIER DE LA SALLE found (1782) that gall stone was soluble in hot alcohol. When the solution was cooled, crystals resembling crystals of boric acid were precipitated. Several years later, in 1814, CHEVREUL was able to isolate a substance found in most gall stones, and named it cholesterin.

Continued researches by subsequent authors show that in most gall stones is also found bilirubin calcium (see FRERICHS 1861). NAUNYN (1892) divided the gall stones into 4 groups: pure cholesterin stones, stratified cholesterin stones, bilirubin calcium stones, and mixed bilirubin calcium stones. This division has on the whole been retained.

In the first half of the 19th century it was thought, as was also done previously, that gall stone, like stone in the kidneys, was formed owing to a congenital, or acquired, predisposition, »diathesis». MECKEL v. HEMSBACH (1856) was the first to point out that gall stone formation was due to a local process taking place in the gall bladder. Gall stone was chiefly made up of cholesterin or pigment calcium, or of both, and these crystalline substances were cemented together by means of an organic binding-medium. He thought that this binding-medium consisted of mucus which had been secreted on account of a »stone-forming catarrh in the gall bladder». EBSTEIN showed (1884) that in renal calculi were found not only salts but also an organic stroma. POSNER and NAUNYN later showed that this was also true of gall stone which consisted of an organic stroma: in the network formed by the stroma, cholesterin and pigment calcium were precipitated.

Relating to the fact that bacteria were discovered to produce infection, the view was expressed that a bacterial infection in the gall bladder would cause gall stone formation, partly by producing the organic stroma and partly by causing such disturbances in the composition of the bile as favoured the precipitation of salts. NAUNYN was the foremost among the scientists who dealt with this problem. He observed that when the gall bladder was inflamed, the bile contained considerably larger amounts of cholesterin than under normal conditions. This increased content of cholesterin was caused by the inflammation: it was due to the epithelial cells being swollen and discharged. The discharged cells got caked and formed a nucleus round which cholesterin and pigment calcium were precipitated. According to NAUNYN's view, the inflammation of the gall bladder was a pre-requisite condition for stone formation, but the latter was rendered easier if, in addition to the inflammation, a hindrance to the emptying of the gall bladder was present. This infection theory, advanced by NAUNYN, stimulated a lively discussion on the formation of gall stone. In

1900, BOYSEN published a paper in which he tried to show that in by far the majority of gall stones, also in pure cholesterin stones, was found a nucleus consisting of pigment calcium. BOYSEN had found small pigment calcium stones in wholly normal gall bladders but cholesterin stones only in inflamed gall bladders. According to the view held by BOYSEN, the infection was important in so far as the pigment calcium stones formed in a non-inflamed gall bladder grew owing to the infection. This theory was partly based on observations made by LANGE (1893). ASCHOFF and BACMEISTER in 1909 published a paper on gall stone in which they propounded the theory that pure cholesterin stones could be formed, and mostly were formed, without the presence of inflammation. They held that this stone formation was caused by disturbances in the cholesterin metabolism. An infection was on the other hand necessary to the formation of other forms of gall stone. ROVSING (1923) agreed with BOYSEN that the primary factor in the formation of gall stone was the formation of bilirubin calcium stone, not in the gall bladder, however, but by precipitation of bilirubin calcium in the liver cells, from which the pigment masses formed were emptied into the gall capillaries and there shaped into small concrements; these could later get into the gall bladder where they grew owing to stratification of cholesterin and pigment calcium. Gall stone in the gall bladder favoured the development of infection, and thanks to the latter the stones were capable of growing further, owing to changes in the composition of the bile caused by the infection.

J. Berg (1922) emphasized the great significance of stasis in the gall bladder to the development of gall stone. BERG was of the opinion that stone was more easily formed in gall bladders, the emptying of which was rendered more difficult on account of anatomical conditions, anomalies, etc.

The discussion relating to the causes of gall stone formation has not led to any conclusive result. We may state that three factors might be important to the formation of gall stone: infection of the gall bladder, hindrance to the emptying of the gall bladder, and disturbances in the metabolism, particularly in the cholesterin metabolism. It is as yet impossible to decide whether one or the other factor has a greater or smaller significance to the formation of gall stone.

The subsequent literature on experimentally produced gall stones,

etc., has not yielded any definite results, either. As the present paper does not deal with the detailed mechanism for the formation of gall stone but aims at giving a clinical survey of the disease, we shall not here give an account of this part of the literature.

*The treatment of gall stone disease.*

Internal treatment of gall stone disease by various drugs, dietetic and hygienic measures, etc., is in a number of cases of no avail. In a comparatively large number of cases, the disease sooner or later leads to serious complications which considerably reduce the capacity for work, cause prolonged states of ill-health, or lead to a fatal issue. ETTMÜLLER (1644—1683) in his day stated that there is no drug which is capable of changing or dissolving gall stones. The experiences of subsequent ages have wholly confirmed this view. On the other hand, we must not, from the fact that many persons suffering from gall stone disease become invalidized, or die from their disease, conclude that internal treatment is hopeless. In point of fact, a comparatively large part of the patients, after careful treatment, will not be much troubled by their disease and may retain their full capacity for work. We shall show below, in the discussion of re-examinations of patients not operated on, that this is the case with about fifty per cent of those who were discharged from hospital after they had been treated for the first time for their disease.

As, however, a large part of the patients could not be cured, or guaranteed a tolerable existence, by internal treatment, it is obvious that surgical treatment of the disease was resorted to in many cases, when, at the end of the last century, it had been shown that the disease could be attacked surgically without too great a risk. During the last decades of the last century, surgical treatment was adopted in the cases where the discomforts were grave and prolonged, especially in the cases where an enlarged and distended gall bladder could be demonstrated, and also in the cases where acute inflammation in the gall bladder and biliary ducts, or obstruction of the common bile duct, forced to operation. The non-complicated cases, particularly those who had less severe discomforts and who had not suffered from their disease over a prolonged period, were as a rule not treated surgically. According as the surgical



methods of treatment were improved and the results of the treatment became more satisfactory, especially in view of the post-operative death-risk, an increasing number of mild cases were also treated surgically.

In the following discussion we shall chiefly deal with the surgical treatment of the gall stone disease, and we shall in the first place give an account of the methods which have been employed.

### *Surgical methods of treatment.*

We have above given an account of the pioneer work which towards the end of the 19th century was carried out on the operative treatment of gall stone disease. The method earliest adopted, the cholecystostomy, used with various modifications, was during the end of the 19th century and up to about the year 1910 the method of operation that was most commonly employed. Among surgeons who exclusively, or almost exclusively, made use of this method, we may mention LAWSON-TAIT (1885), MAYO ROBSON (1897), LENNANDER (1893), ROVSING (1899, 1911, 1924) DEEVER (1906), TSCHERNING (1911), BORCHGREVINK (1911). Cholecystostomy still longer held its ground as the most current method of operation in England and America.

In Germany and Switzerland, however, cholecystectomy began to be performed at an early date. In the eighties it was performed to a comparatively large extent by LANGENBUCH, the inventor of this method, and by COURVOISIER. In 1890, the latter was able to report on 47 cases, 5 of which he had operated on himself. In the nineties, the method gained many enthusiastic followers, among whom KEHR, KÖRTE and RIEDEL before long became the leading surgeons of the biliary tract diseases. In the Scandinavian countries the first cholecystectomy was performed by BERG 1891. Towards the end of the nineties, BORELIUS in Lund began to employ cholecystectomy as standard method in operation for gall stone disease and became one of the most energetic supporters of this method in Scandinavia.

In the years after 1910, cholecystectomy was commonly adopted as the standard method for operative treatment of gall stone disease (DEEVER 1913, C. H. MAYO 1914, KEHR 1913, etc.). Cholecystostomy, however, was adopted in certain cases, especially in operation of advanced cases of acute cholecystitis, where it is still used to a

certain extent, in recent years in an increasing number of cases. In this connection it may be mentioned that cholecystostomy has been more and more used in recent years as the method of operation in cases of jaundice due to hepatitis. (UMBER 1919, ROVSING 1924, v. HABERER 1932, CAROLI and BENOIT 1935 a. v.)

**Indications for surgical treatment.** In the year 1890, COURVOISIER formulated the indications for surgical treatment of the gall stone disease as follows: an operative interference is indicated in the case of severe and persistent discomforts which resist internal treatment, further in cases of stone in the common bile duct, of empyema in the gall bladder, and finally in cases of perforation of inflamed gall bladder. These indications for surgical treatment have on the whole been adhered to ever since. The subsequent discussion has mainly developed along two lines. The authors have discussed what cases ought to be subjected to internal treatment, and what cases ought to be operated upon. Further, the suitable time at which the operation should be made has been discussed.

**Acute cholecystitis.** NAUNYN, who in the nineties was the leading internal specialist in the field of gall stone diseases, pointed out as early as 1892 that cases of acute cholecystitis should now and then be treated surgically, especially the severe cases. As time went on, he became more and more conservative, however, because he had on repeated occasions observed that even severe cases of acute cholecystitis may recover without operation. In surgical quarters, on the other hand, it was maintained in the nineties that a comparatively large number of cases of acute cholecystitis ought to be operated on. KEHR (1899) operated on the cases in which it was possible to palpate a resistance at the site of the gall bladder. LENNANDER, who as early as 1893 published his first operations for gall stone disease, operated if the cholecystitis was serious from the start, or if the symptoms did not rapidly subside. As late as the beginning of the 20th century, however, surgeons were rather reluctant to operate on cases of acute cholecystitis during the acute stage as it was thought that a risk was present that the infection, restricted to the gall bladder, would then spread in the abdominal cavity. RIEDEL (1903) and KÖRTE (1902) showed, however, that this risk was exaggerated and they insisted that every case of acute cholecystitis ought to be operated

on, and operated on in the acute stage. Equally advanced views were held by LEJARS (1902) and MOYNIHAN (1908). As a rule, however, surgeons were comparatively reluctant during the first decade of the 20th century to operate on cases of acute cholecystitis. The severe, and the most severe, cases were operated on (MURPHY, 1903, TÖRNQVIST, 1903, and KROGIUS, 1906) as also the cases in which the symptoms did not rapidly subside.

In the continued discussion it turned out that the majority of the surgeons thought that cases of acute cholecystitis ought to be operated on, but the discussion was more and more centred on the suitable time at which an operation should be performed. KEHR, who previously operated during the acute attack, as early as 1906 had arrived at the view that attempts should be made to make the acute attack abate under conservative treatment in order later to operate in the stage of the free interval. In the cases in which the acute symptoms had not subsided after a week, it was advisable to operate, however, as in the most severe cases. At the international surgical congress in Brussels in 1908, QUÉNUE and DUVAL were of the same mind as KEHR, whereas MOYNIHAN operated during the acute stage. KÖRTE (1909) and RIEDEL (1908) also advocated that the cases of acute cholecystitis ought to be operated on as early as possible, while ARNSPERGER (1908) preferred to operate in the stage of free interval. PAUS in 1912 expressed the view that attempts ought to be made to arrive at a more individualizing treatment. The most severe cases ought to be operated on. In other cases expectant treatment might be adopted until the disease had entered upon a more chronic stage, when operation should be performed. In the mildest cases it was not necessary to operate.

At the Scandinavian surgical meeting in 1916 the question of the treatment of acute cholecystitis was discussed. BORELIUS, like J. BERG, PAUS and ROVSING, advocated the view that operation ought to be performed as early as possible during the acute attack. In the continued discussion KIRSCHNER (1918) pointed out that the severe cases ought to be operated on immediately but the other cases only when the acute symptoms had subsided.

At the German surgical congress in 1923, HOTZ presented a large statistical survey and showed that operation during the acute attack resulted in a mortality of 13,1 per cent, whereas the mortality of operation in the free interval was only 6,8 per cent. In a dis-

cussion on the therapy of gall stone disease in the periodical »Medicinische Klinik» in 1924—1925, the internists KUTTNER, MORAWITZ, and others, proved to be fairly agreed that operation should be performed during the acute attack only in the most severe cases. From internal quarters it was pointed out that the mortality after operation in the acute stage, according to HOTZ, was considerably greater than during the stage of interval and that, consequently, it would be of advantage to avoid operation in the acute stage. Among surgeons who contributed to this discussion, STICH, FINSTERER, KIRSCHNER and others were of the opinion that operation ought to be performed early during the acute attack, whereas SCHMIEDEN, ENDERLEN, HOTZ, and others preferred to operate during the interval. The question as to the suitable time at which operation for acute cholecystitis should be performed has subsequently been eagerly discussed, and the discussion still goes on. In summarizing we may state that American surgeons to a large extent advocated early operation whereas surgeons in Scandinavia and Germany preferred to operate after the acute symptoms had subsided. In recent years it has been advocated in the latter countries also that operations should be performed to a larger extent during the acute attack (PETRÉN, LIEBERG). In chapter VI we shall give a more detailed account of the discussion held in the last decades as to the suitable time at which operation for acute cholecystitis should be performed.

Stone in the common bile duct. In the nineties operations for common duct stone were performed in the cases in which the patient had severe jaundice or cholangitis. Such cases have ever since been subjected to surgical treatment, and it has actually never been discussed whether these cases should be operated on or not. The discussion has instead been centred partly on the time most suited to an operation in such cases, and partly on the extent to which the common bile duct ought to be explored in other cases in which, owing to anamnestic or clinical symptoms, there is reason to suspect common duct stone. As early as the end of the nineties, KEHR pointed out that the operator ought to open the common duct in a comparatively large number of cases in order to find out whether it held stones. In a series of papers in the first decade of the 20th century, he eagerly advocated that choledochotomy ought to be performed more and more, followed by hepatic drainage. A comparatively great risk was present that common



duct stones might otherwise be overlooked, as such stones might be present without giving clinical symptoms or being palpable in the common duct in the operation. In 1912, KEHR formulated his indications for choledochotomy as follows. He performed choledochotomy in the cases in which common duct stone could be diagnosed or was suspected (jaundice, chills, or passage of stone in the anamnesis, dilated common duct with thick walls, thickened pancreas or cases in which turbid bile was passed through the cystic duct). He further made choledochotomy in the cases in which he found many small stones in the gall bladder and in the cystic duct. These wide indications for choledochotomy met with opposition in many quarters.

BORELIUS, in 1911, thus pointed out that choledochotomy was such a serious interference that it only ought to be made in cases in which stone in the common duct could be diagnosed or in which there was a well-grounded suspicion to that effect. RIEDEL, like CRILE (1914), were also reluctant to perform choledochotomy. During the following decades the majority of the surgeons were of the opinion that choledochotomy ought to be performed only in the cases in which the presence of a common duct stone was to be assumed. J. BERG (1923), for instance, considered that a widened common bile duct indicated choledochotomy. PETRÉN (1927) also performed choledochotomy only in the cases which held a suspicion of stone in the common duct. However, individual surgeons had early begun to perform choledochotomy on wide indications in agreement with KEHR, as for instance KÖRTE (1909). NORDMANN (1921) performed choledochotomy on wide indications and had found common duct stone in 22 out of 97 cases, operated on for acute cholecystitis. Of the 22 cases, more than fifty per cent had not had jaundice either in the anamnesis or during the stay in the hospital. HEIDENHAIN (1921) also performed choledochotomy to a comparatively large extent.

In the last decade, the importance of exploring the common duct to a larger extent than previously has been emphasized, particularly by American authors. One cause of this is the fact that, in operations for relapse, stones have not infrequently been found in the common bile duct. As it is fairly commonly held that stone is not primarily formed in the common duct, such a stone must have been overlooked in a previous operation. In proportion as choledoch-

tomy began to be adopted to a larger extent, stone in the common duct was found in a relatively larger number of cases than before. CLUTE (1930), who in recent years had begun to perform choledochotomy to a larger extent than previously, found relating to these operations an increase in the observed number of common duct stones from 8,4 per cent up to 17,9 per cent. LAHEY (1930) had had a similar experience: he had earlier made choledochotomy on strict indications and found common duct stone in 8,4 per cent of the cases, whereas he found such stone in 21,2 per cent after the indications had been widened. Examinations of autopsy materials have further shown that stone in the common bile duct are present comparatively often in the cases where stone is found in the gall bladder. CRUMP thus found common duct stone in no less than 21 per cent of the cases in which stone was present in the gall bladder. In the last years when X-ray examinations of the biliary ducts have begun to be performed during the actual operation (e. g. MIRIZZI, DESPLAS, MOULONGUET and MALGRAS, HULTÉN), stone in the common duct has frequently been observable in cases in which, on the basis of clinical symptoms or operation findings, it was considered that the presence of such stones could be excluded. As, further, experience in recent years has shown that the risk of explorative choledochotomy has probably been overestimated (e. g. CLUTE and SWINTON 1934, and others), an increased tendency to explore the common bile duct to a larger extent has begun to assert itself, even in cases where neither anamnesis nor clinical symptoms seem to indicate the presence of stone in the common duct.

In the case of patients presenting clinical symptoms of common duct stone, the tendency in early years was to stand expectant for some time in the cases without fever, before operation was performed. PETRÉN (1925), however, showed that after jaundice had been present for more than three weeks, there was a great risk of cholemia and that, accordingly, operation ought, if possible, to be performed within the three first weeks after the appearance of symptoms of obstruction in the common bile duct. In surgical quarters the tendency in recent years has been to subject the patients to treatment in a comparatively early stage of the disease (HEIDENHAIN, 1921, PETERMANN, 1926, KROGIUS, 1931, and others). In the cases attended by fever, the indication for operation has proceeded along fairly parallel lines

with the indications for operation in acute cholecystitis. It has been claimed more and more that these patients should be operated on in an early stage of the disease (e. g. HEIDENHAIN, ANSCHÜTZ, FINSTERER.)

REIMANN found in 1917 that the liver showed inflammatory changes in cholecystitis. GRAHAM (1918), CAVE (1926), BEHREND (1927), ALBOT and CAROLI (1931), and others have later on examined the acute liver changes which are often present at acute inflammatory processes in the gall bladder and biliary ducts. On account of this, attention has been more and more called to the importance of a »liver-preserving» therapy in acute inflammatory conditions of the gall bladder and biliary ducts. MAYO (1921) pointed out the significance of administering plenty of glycosis in cases which hold a suspicion of a disturbance in the liver function, particularly in common duct stone and acute cholecystitis. The importance of an abundant supply of sugar in such cases has later been generally recognized and has no doubt to a certain extent contributed to the fact that the results of treatment for stone in the common bile duct have been improved during the last decades as compared to previous years.

**The chronic cases.** In the cases of gall stone disease in which the patient has often severe attacks, it is true, but where the disease is not directly threatening to life, operations were to begin with performed on fairly strict indications. Around the year 1900 the attitude was this: these patients were as a rule treated by internists and operation was recommended only when internal treatment proved to be of no avail. We have previously mentioned that NAUNYN was on the whole very conservative as regards surgical treatment of gall stone disease. In the chronic cases, this conservative attitude was favoured by the fact that cholecystostomy was made in a large number of cases in the nineties. After this operation, relapses proved to be fairly frequent, and the possibility of curing the patient after surgical treatment was not considered to be very great (NAUNYN, HERRMAN, 1899). Cholecystectomy soon proved to involve a considerably smaller risk of relapse. In proportion as this method of operation began more and more to be used as the standard method, there was an increase in the number of chronic cases operated on. Among surgeons, fairly divergent views were to begin with held on the extent to which gall stone patients

ought to be operated on. RIEDEL (1903) acted on extremely wide indications and held that 90 per cent of the cases ought to be operated on. KEHR, on the other hand, who in his time had the greatest personal experience of surgical treatment of gall stone disease, thought operation to be indicated only in about 20 per cent of the cases. At the abovementioned international surgical congress in Brussels in 1908, KEHR *inter alia* expressed his above mentioned views on the treatment of chronic cases. MOYNIHAN, on the other hand, like BRÜNING, was of the opinion that chronic cases ought also to be operated on to a very large extent. The same radical attitude was also adopted by RIEDEL and KÖRTE (1909), ROVSING (1916) and KIRSCHNER (1918). Other surgeons were more abstemious as regards operation of these cases. RINGEL and KLEIN-SCHMIDT (1923) held that the non-complicated cases need not as a rule be operated on. At the German surgical congress in 1923, HOTZ, as mentioned above, showed that the mortality after operation in the stage of interval was considerably lower than during the acute attack. ENDERLEN advocated the view that the patients should be operated on at an early stage of the disease and in early years. In the discussion in the Medizinische Klinik in 1924—1925, however, the internists were as a rule not inclined to operate on the chronic cases. UMBER pointed out that he had thought operation to be indicated only in 4.4 per cent of his 771 patients with gall stone disease. VOIT, KÜTTNER, and others expressed similar views. KREHL, on the other hand, was the most active among the internists. Among the surgeons, ENDERLEN and HOTZ adhered to the principle expressed by Enderlen in 1923: »Frühoperation in jungen Jahren«. KÜTTNER and ANSCHÜTZ adopted a similar attitude whereas certain objections were raised from other surgeons, for instance DE QUERVAIN and PERTHES, who held that it was not necessary to operate on non-complicated cases. In the continued discussion KIRSCHNER (1924) insisted that »jedes Gallensteinleiden, sobald es mit Sicherheit als solches erkannt ist, bei einem sonst gesunden, noch im rüstigen Alter stehenden Menschen ist chirurgisch zu behandeln«. KÖRTE (1924), on the other hand, pointed out that regard should be paid to the fact that the risk of an operation was not so inconsiderable that on this account the indications should be widened for operation of the non-complicated cases. After ENDERLEN's and HOTZ's papers had been published in 1923,



the discussion has to a large extent been centred on the question as to whether operation should be performed during the acute attack or in the interval. By the stage of interval is often denoted the stage of the disease in which, after an acute attack, the clinical symptoms have subsided, the tenderness has disappeared, and the temperature has become normal (ANSCHÜTZ, 1927). Operation of more chronic cases, in which no really acute attack has occurred, has also been termed operation in the interval. It is often difficult to obtain figures from the literature for the risk of operation of chronic cases, as these two groups of operations in the interval are often brought together.

At the meeting of the Scandinavian Surgical Association in 1931, when indications for the treatment of gall stone disease were discussed, KJAERGAARD pointed out that a comparatively large number of the non-complicated cases were capable of healing without operation and that, consequently, it was not indicated to operate on the less severe cases. KROGIUS held the same views as regards the chronic cases and considered operation to be indicated if the attacks became frequent or were complicated by jaundice.

In recent years, American surgeons in particular have operated on chronic cases to a considerably larger extent than previously (MENZER, 1932, JUDD and PHILLIPS, 1933, HEUER, 1934, and others). In the published materials, however, are often included a large number of cases in which stone was not found in the gall bladder and which are characterized as »non-calculous cholecystitis».

In summing up it should be pointed out, in regard to the early literature on the treatment of the gall stone disease, that the authors largely based their views on series of operations, or series of conservatively treated patients, but that they did not submit their materials to a close statistical analysis. The series of figures given are often small and no attempts have been made to try to establish to what extent random variations might have played a part in causing a displacement between the series of figures. As the materials are small, this shortcoming is hardly of any great importance, however: even if the materials had been analysed statistically, they would hardly have been capable of yielding definite conclusions, the more so as different series of operations are rarely fully comparable and as, further, the data referring to the materials are in a way incomplete (particularly when no information is given as to what part of

the material was treated surgically and what part was treated internally). To this should be added that the early figures refer to a current technique of operation — this term is applied not only to anesthesia and operation but also to the treatment before and after the operation — which is not comparable with the one nowadays employed. This being so, we have refrained from giving a more detailed account of the early materials and from criticism of minor points, but are content to give a general survey of the various views held on the rational treatment of the gall stone disease.

Only when we come to a more recent time is it of interest to examine in detail the literature on this subject. In the foregoing pages an account has been given of the divergent views expressed in recent years. Attempts have been made, on the basis of figures obtained from series of operations, to justify the different lines of treatment adopted. In regard to these computations of figures a criticism may be advanced similar to the one applying to the publications of earlier writers in this field. The material has not been closely analysed from a statistical point of view. Two defects are apparent: on one hand, hardly any attempts have been made to establish to what extent random variations may cause displacements and whether the materials are large enough to allow of any conclusions; on the other hand, hardly any attempts have been made, either, to analyse to what extent selective factors may be important and to what extent desolate cases have been removed. As a rule no information is given as to the part of the material that has been submitted to surgical treatment and the number of cases that have been treated internally, nor as to the possible mortality in the latter group of cases.

The object of the present investigation is to try to analyse in a more satisfactory manner a material of gall stone cases and to consider these different sources of error. With regard to the conclusions that may possibly be drawn from our own material, it is necessary to compare the latter with the materials presented in the literature. In order to avoid repetition, we have therefore, in the above survey of the investigations so far published, not discussed in detail the series of figures on which are based the views on indications etc., and we have not submitted these views to a detailed criticism. Such a comparative analysis of the materials presented by earlier authors will be given in connection with the discussion of the results arrived at on the basis of our own material.

In the literature investigations into a total material of gall stone cases are lacking, with regard to the result of the treatment for the actual attack that brought the patient to the hospital, whether operative or not, and with regard to the subsequent histories of the patients from the viewpoint of risk of relapse. Further, data are lacking on the magnitude of the actual risk for a patient with gall stone disease at different ages, by internal or surgical treatment of the disease. Finally, the investigations dealing with the occurrence of gall stone relative to the morbidity and mortality of the gall stone disease are infrequent and, in our opinion, open to objections.

## CHAPTER 2.

### **The Material.**

The material on which the present investigation was based, has been collected from different sources:

- 1) Data on causes of death taken from the official statistics;
- 2) Autopsy material from the Pathological Institution in Uppsala;
- 3) Clinical material of cases of gall stone disease from the surgical department of the Academical Hospital in Uppsala.

1) As regards the official statistical data on causes of deaths it should be pointed out that the Swedish data on deaths in towns are more reliable than the corresponding data for the country, because in towns, a death-certificate issued by a licensed physician has to be presented in a case of death. Consequently, the data obtained from the population statistics for Swedish towns are fairly correct. In the official statistics, the gall stone disease is not recorded separately but together with the liver diseases. Through the kind courtesy of the Central Statistical Bureau in Stockholm we have been able, however, to obtain figures on deaths from gall stone and inflammation of the gall bladder in Swedish towns for the years 1931—1935.

In the records kept at the Central Statistical Bureau, deaths from gall stone disease are subdivided into deaths from gall stone and deaths from inflammation of the gall bladder. This division naturally is not very reliable: the line of demarcation between gall stone disease in a restricted sense (cholelithiasis), and inflammation of the gall bladder, is not always easy to draw, especially not for a general practitioner who is less familiar with surgical diseases. The sum of deaths both from gall stones and inflammation of the gall bladder, however, must be considered to give a fairly reliable expression of the actual mortality of the gall stone disease. Of the material of deaths with the clinical picture of gall stone disease in the clinic in Uppsala during the years 1922—1935, comprising 71 cases, 66 cases



presented gall stone, and 5 cases had no stone. Stone was accordingly absent in 7.0 per cent of the deaths. On this account it is to be expected that among those who were recorded as having died of gall stone disease in the official statistics, there is a small number of cases which did not have gall stone.

2) The autopsy material belongs to the Pathological Institution in Uppsala and consists of the autopsies being recorded in the years 1929—1936. These autopsy cases consist of deaths which occurred in the Academical Hospital, that is to say the hospital to which our clinical material belongs. Among the post-mortem examinations are included some cases which had previously been operated on for gall stone disease, when gall stones and possibly the gall bladder were removed. In these cases gall stone was naturally not found in the post-mortem examination, but as stones had been present earlier we have counted these cases among those which were found to contain gall stones at the post-mortem examination.

To a certain extent the material constitutes a selection, as we are concerned with persons who have died in hospital from the one or the other disease. It may be imagined that the frequency of gall stones among living persons is different from the one found in an autopsy material of this type. In order to obtain an idea of the extent to which the autopsy material is a selection, we calculated the percentage of the post-mortem examinations falling in the various age groups. A similar calculation was made for the number of deaths in the province of Uppsala (the region in which the deceased were domiciled). The figures thus obtained show a remarkably good accordance with the exception only of the highest age groups which are represented in the autopsy material to a somewhat less extent (see table 1 and fig. 1). As the relation between the deaths in different age groups is practically identical in the autopsy material and in the population, we must infer that the autopsy material is fairly representative of the population. We thus have reason to expect that the figures for the frequency of gall stone which are to be obtained from the autopsy material, should not deviate too much from those which refer to the population.

3) The clinical material was obtained from the surgical department of the Academical Hospital in Uppsala. It comprises all the cases of gall stone disease which were treated in the hospital during the years 1922—1935. Some patients come to treatment in the medical de-

Table 1. *Comparison between percentage distribution in each year group of all deaths in autopsy material from the Pathological Institution in Uppsala and in the population in the province of Uppsala.*

| Age   | Autopsy material<br>1929—36 | Deaths in<br>Uppsala prov.<br>1929—36 |
|-------|-----------------------------|---------------------------------------|
| 0—9   | 13,7                        | 8,7                                   |
| 10—19 | 4,9                         | 2,7                                   |
| 20—29 | 8,5                         | 4,5                                   |
| 30—39 | 7,8                         | 4,3                                   |
| 40—49 | 9,8                         | 5,7                                   |
| 50—59 | 14,3                        | 8,3                                   |
| 60—69 | 18,3                        | 16,3                                  |
| 70—79 | 17,1                        | 26,2                                  |
| 80—   | 5,6                         | 23,4                                  |
| Total | 100,0                       | 100,0                                 |

partment. As a rule they are transferred to the surgical department when operation is contemplated, or else they come to treatment in the surgical department at a recurrent attack. In order to obtain an idea of the number of cases of gall stone disease which were treated in the medical department and were not subsequently treated in

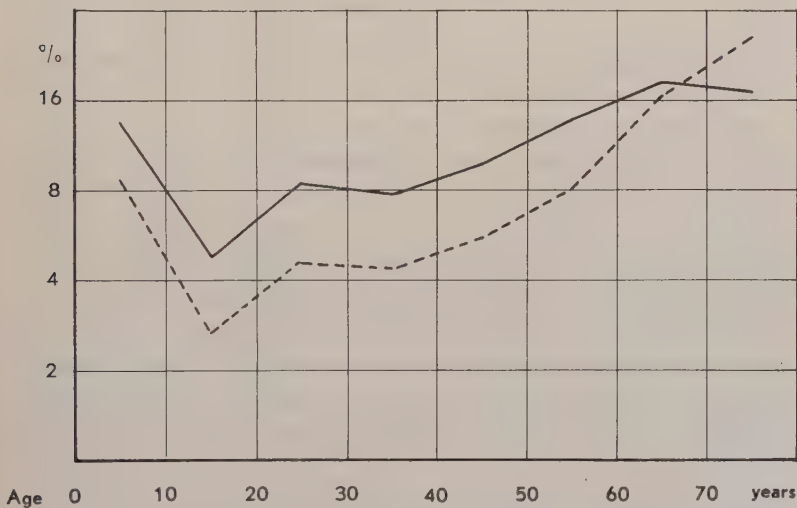


Fig. 1. Number of cases at different ages among 100 deaths in the autopsy material from Uppsala (unbroken line), and from the province of Uppsala (broken line) during the years 1929—1936 (cf. table 1).

the surgical department, we collected the cases which were treated in the medical department during the 9 years between 1922 and 1930. During this long period, only 35 cases were not transferred to, or later treated in, the surgical department. These patients mostly suffered from another disease for which they came to treatment; the gall stone disease in most cases did not dominate the picture of disease.

The diagnosis naturally is quite clear in the cases operated on. In the patients not operated on, the diagnosis may on the other hand be more or less uncertain in some cases. This particularly applies to that part of the material which refers to the time before 1929, that is the year in which the cholecystographic examination began to be adopted in the hospital. The acute cases of cholecystitis, with a temperature of  $38^{\circ}$  C or more, accompanied by tenderness, rigidity and usually resistance at the site of the gall bladder, do not give cause for any doubt as to the diagnosis. In some cases of non-complicated cholelithiasis, on the other hand, the symptoms may be so vague that the diagnosis can only be made with a certain hesitation. No other cases were included, however, than those presenting both a typical anamnesis and typical symptoms (tenderness over the gall bladder, possibly tenderness on percussion over the liver border, or jaundice and in some cases a positive X-ray finding in the form of enlarged gall bladder, impression of the duodenal bulb, stones, or deficient contrast filling). The cases in which the diagnosis seemed to be at all uncertain were not included in the material.

As pointed out above (cf. p. 8), the cases operated on for acute or chronic cholecystitis in which gall stone was not found, were not included in the material. It is probable that among the cases not operated on are included some cases which presented clinical symptoms of gall stone disease but had no gall stone. For reasons stated above, the number of such cases is probably fairly small.

The clinical material consists of 1061 cases, 211 men and 850 women. The distribution of the material on cases not operated on, and cases operated on, during the first stay in hospital, and the distribution of the cases operated on on different forms of the disease, appear in table 2.

Table 2. The clinical material of persons suffering from gall stone disease. Year of first stay in hospital, and deaths.

| Year<br>of first<br>stay | Not operated   |                       |        |                       |        |                       | Operated       |                       |        |                           |        |                       |                        |                       |        |                         |        |                       | Not op. + op. |    |           |                       |        |                       |        |                       |    |    |     |    |     |    |     |    |
|--------------------------|----------------|-----------------------|--------|-----------------------|--------|-----------------------|----------------|-----------------------|--------|---------------------------|--------|-----------------------|------------------------|-----------------------|--------|-------------------------|--------|-----------------------|---------------|----|-----------|-----------------------|--------|-----------------------|--------|-----------------------|----|----|-----|----|-----|----|-----|----|
|                          | Cholelithiasis |                       |        | All cases             |        |                       | Cholelithiasis |                       |        | Cholecystitis<br>chronica |        |                       | Cholecystitis<br>acuta |                       |        | Cholechohli-<br>thiasis |        |                       |               |    | All cases |                       |        |                       |        |                       |    |    |     |    |     |    |     |    |
|                          | M.             |                       | W.     | M.                    |        | W.                    | M.             |                       | W.     | M.                        |        | W.                    | M.                     |                       | W.     | M.                      |        | W.                    |               |    | M.        |                       | W.     | M.                    |        | W.                    |    |    |     |    |     |    |     |    |
|                          | Number         | deaths among<br>these | Number | deaths among<br>these | Number | deaths among<br>these | Number         | deaths among<br>these | Number | deaths among<br>these     | Number | deaths among<br>these | Number                 | deaths among<br>these | Number | deaths among<br>these   | Number | deaths among<br>these |               |    | Number    | deaths among<br>these | Number | deaths among<br>these | Number | deaths among<br>these |    |    |     |    |     |    |     |    |
| 1922                     | 1              | —                     | 3      | —                     | 2      | —                     | 4              | —                     | 3      | —                         | 7      | —                     | 6                      | —                     | 1      | —                       | 5      | —                     | 2             | 1  | 11        | 1                     | —      | 2                     | —      | 3                     | 1  | 24 | 1   | 6  | 1   | 31 | 1   |    |
| 1923                     | 1              | —                     | 4      | —                     | 3      | —                     | 10             | 1                     | 4      | —                         | 14     | 1                     | 11                     | —                     | —      | —                       | 1      | —                     | —             | 8  | 2         | 2                     | 2      | —                     | 5      | —                     | 2  | —  | 25  | 2  | 6   | —  | 39  | 3  |
| 1924                     | —              | —                     | 2      | —                     | 3      | 1                     | 9              | 1                     | 3      | 1                         | 11     | 1                     | 9                      | —                     | 2      | 1                       | 1      | —                     | 6             | 4  | 8         | 1                     | 1      | 1                     | —      | 5                     | —  | 5  | 23  | 1  | 12  | 6  | 34  | 2  |
| 1925                     | —              | —                     | 6      | —                     | 5      | —                     | 18             | 1                     | 5      | —                         | 24     | 1                     | —                      | —                     | —      | —                       | 5      | —                     | —             | 10 | 1         | 1                     | 1      | —                     | 5      | —                     | 1  | —  | 32  | 1  | 6   | —  | 56  | 2  |
| 1926                     | 3              | —                     | 8      | —                     | 2      | —                     | 17             | —                     | 5      | —                         | 25     | —                     | 12                     | —                     | —      | —                       | 4      | —                     | —             | 17 | 2         | 3                     | 1      | 3                     | 1      | 6                     | 1  | 36 | 3   | 10 | 1   | 61 | 3   |    |
| 1927                     | 4              | —                     | 5      | —                     | 6      | —                     | 9              | 2                     | 10     | —                         | 14     | 2                     | —                      | —                     | 1      | —                       | 8      | 1                     | 4             | —  | 15        | 1                     | 1      | —                     | 6      | 1                     | 6  | —  | 38  | 3  | 16  | —  | 52  | 5  |
| 1928                     | 4              | —                     | 6      | —                     | 10     | —                     | 13             | 1                     | 14     | —                         | 19     | 1                     | 7                      | —                     | 1      | —                       | 9      | —                     | 7             | 1  | 20        | 1                     | —      | —                     | 7      | 3                     | 9  | 1  | 43  | 4  | 23  | 1  | 62  | 5  |
| 1929                     | 1              | —                     | 11     | —                     | 3      | 1                     | 15             | —                     | 4      | 1                         | 26     | —                     | 9                      | —                     | 2      | —                       | 6      | —                     | 18            | 3  | 2         | 1                     | 3      | 1                     | 3      | 1                     | 7  | 1  | 36  | 4  | 11  | 2  | 62  | 4  |
| 1930                     | 5              | —                     | 11     | —                     | 10     | 1                     | 12             | 1                     | 15     | 1                         | 23     | 1                     | 3                      | —                     | 1      | —                       | 3      | —                     | 3             | 2  | 15        | 2                     | 2      | 1                     | 10     | —                     | 10 | 3  | 44  | 3  | 25  | 4  | 67  | 4  |
| 1931                     | 2              | —                     | 20     | —                     | 7      | —                     | 20             | 2                     | 9      | —                         | 40     | 2                     | 2                      | —                     | —      | —                       | 3      | —                     | 2             | —  | 10        | 1                     | 1      | —                     | 3      | —                     | 5  | —  | 25  | 1  | 14  | —  | 65  | 3  |
| 1932                     | 4              | —                     | 13     | —                     | 9      | 2                     | 27             | 1                     | 13     | 2                         | 40     | 1                     | 1                      | —                     | —      | —                       | 4      | 2                     | 1             | —  | 16        | —                     | —      | —                     | 3      | 1                     | 2  | —  | 34  | 3  | 15  | 2  | 74  | 4  |
| 1933                     | 6              | —                     | 18     | —                     | 6      | —                     | 21             | 2                     | 12     | —                         | 39     | 2                     | 3                      | —                     | —      | —                       | 7      | —                     | 4             | —  | 15        | 1                     | 2      | —                     | 7      | 2                     | 9  | —  | 42  | 3  | 21  | —  | 81  | 5  |
| 1934                     | 4              | —                     | 23     | —                     | 9      | —                     | 21             | 2                     | 13     | —                         | 44     | 2                     | —                      | —                     | —      | —                       | 3      | —                     | 2             | —  | 20        | 2                     | 1      | —                     | 7      | —                     | 4  | —  | 40  | 2  | 17  | —  | 84  | 4  |
| 1935                     | 10             | —                     | 14     | —                     | 13     | —                     | 25             | 1                     | 23     | —                         | 39     | 1                     | —                      | —                     | 3      | —                       | 5      | —                     | 2             | —  | 19        | —                     | 1      | —                     | 5      | —                     | 6  | —  | 43  | —  | 29  | —  | 82  | 1  |
| Total                    | 45             | —                     | 144    | —                     | 88     | 5                     | 221            | 15                    | 133    | 5                         | 365    | 15                    | 13                     | —                     | 148    | 1                       | 164    | 3                     | 35            | 8  | 202       | 18                    | 17     | 3                     | 71     | 9                     | 78 | 19 | 485 | 31 | 211 | 17 | 850 | 46 |



## CHAPTER III.

### Statistical Methods.

In the treatment of the material the following formulas were employed: The standard deviation,  $\sigma$ , was calculated according to the formula:

$$\sigma = \pm \sqrt{\frac{\sum a^2}{n-1}}$$

where  $a$  = the deviation from the mean, and  $n$  = the number of variants.

The standard error of a mean,  $\varepsilon(M)$ , was calculated according to the formula:

$$\varepsilon(M) = \pm \frac{\sigma}{\sqrt{n}}$$

where  $\sigma$  = the standard deviation, and  $n$ , as in the first formula, is the number of variants.

The standard error of a percentage value,  $\varepsilon(p)$ , was calculated according to the formula:

$$\varepsilon(p) = \pm \sqrt{\frac{p(100-p)}{n}}$$

The standard error of a difference,  $\varepsilon(D)$ , was calculated according to the current formula:

$$\varepsilon(D) = \pm \sqrt{m_1^2 + m_2^2}$$

where  $m_1$  and  $m_2$  = the standard error of the means on the basis of which the difference was obtained.

A difference which amounts to at least 3 times the standard error was considered to be statistically significant. If the difference amounts to  $2\frac{1}{2}$ —3 times the standard error, it was denoted as probable.

## CHAPTER 4.

### **Gall Stone and Gall Stone Disease from a Demographic Point of View.**

Gall stone occurs at all ages even in new-born children. In order to obtain an idea of the frequency of gall stone at different ages, in men and women, examinations have been made with a view to finding out how often gall stone is found in autopsy materials. These investigations show that gall stone is present with a frequency increasing with rising age. If we assume that the autopsy materials examined are representative of the population to which they refer, we have reason to expect that the frequency of gall stone in the population also increases with rising age. This means that there exists a risk of developing gall stones, a risk applying to all age groups. We do not know the magnitude of this risk.

Only part of those who develop gall stones, also get symptoms of gall stone disease. Both in examinations of autopsy materials and in operations for other diseases than gall stone disease (e. g. W. J. MAYO, 1911, PETERSON, 1915, TRUESDELL, 1933), numerous cases have been found in which, so far as is known, gall stone never gave clinical symptoms.<sup>1)</sup> Similar observations have been made in X-ray examinations. The risk of contracting gall stone disease consequently must be smaller than the risk of developing gall stone.

As the risk of contracting gall stone disease is smaller than the risk of developing gall stone, we might ask what is the relation between these two risks.

The mortality of the gall stone disease is much debated. Investigations have been made into the mortality of certain forms of gall stone disease, particularly of acute cholecystitis. The mortality of gall stone patients at different ages has further been examined.

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<sup>1)</sup> It may here be mentioned that the celebrated K. G. Lennander, late head of the surgical department in Uppsala (to which our clinical material belongs), had gall stone without clinical symptoms.

Attempts have principally been made to get a conception of the mortality of certain forms of gall stone disease when the patients are treated in one way or another. However, there exists no investigation into the risk of dying from the gall stone disease in a total material, comprising cases both operated on and not operated on, of the different forms of the disease, in which different sexes and age groups are considered. Further, no attempts have so far been made to obtain an idea of the risk of dying from gall stone disease from the point of view of the population.

If we want to treat gall stone and gall stone disease from the point of view of the population and to get a conception of the different risk factors that may be present, the following questions should, if possible, be answered:

- 1) What is the risk of developing gall stone?
- 2) What is the risk of contracting gall stone disease?
- 3) What is the risk of dying from gall stone disease?

All these risks should be calculated for men and women, and for different ages.

We may relate these risk figures to one another, and ask:

- 4) What is the risk of contracting gall stone disease for a person with gall stone? (Conversely, what is the risk of having gall stone without presenting clinical symptoms of gall stone disease?)
- 5) What is the death-risk for a person suffering from gall stone disease?

These formulations of the problem are theoretically simple and clear, but it is not so easy to obtain material on which to solve them. The reason why the compilations as yet published have offered no answers to these questions may partly be sought in this very difficulty. We shall try to answer the questions proposed on the basis of the materials at our disposal.

In the following, calculations have been carried out in somewhat different manners. We have dealt with frequencies in certain age groups in one-time observations. This applies to the autopsy material in which individuals at varying ages were observed at the time of death. We have further dealt with frequencies during a given period of time for certain events, for instance when, on the basis of anamnestic data, we have built up frequencies of attacks of gall stone disease in persons of a given age during one year. In comparing the tables we must distinguish between these frequencies,

which are different in character. When we are concerned with frequencies of events having occurred during a given period of time, we speak of risks or risk figures. Strictly speaking, however, a risk figure denotes the potential occurrence of certain events in a material which is observed over a certain period of time. For instance, when we are concerned with the death-risk, we proceed as follows. A certain group of persons are observed from the beginning of a year until the end of a year, and the number of deaths are calculated in per cent of the number of persons at the beginning of the year. The risk figures we use for the mortality are somewhat different in character. In point of fact they are central quotients. We have the number of deaths during a given year among persons of a given age, and relate this number to the average population within this age group. The difference is this: the number of deaths are related to the average number of living persons during the year, and not to the number of living persons at the beginning of the year. The difference between a central quotient calculated in this way and a risk figure in the proper sense of the word, however, is in many cases not really important and should be of no significance to the present investigation, as we are here throughout concerned with approximate calculations. We emphasize these points of view only in order to arrive at a clearer and more logical definition of the problem.

### **1. The risk of developing gall stone from the point of view of the population.**

In the literature we find several data on the frequency of gall stone, obtained in autopsy materials. In many cases information is only given as to the percentage of gall stones in men and women. It is obvious that such data can only be compared with one another on the supposition that gall stone occurs equally frequently in each age group. If, on the other hand, the frequency of gall stones differs in different age groups, a material including a comparatively large number of persons belonging to an age group in which gall stone is common, must contain a greater percentage of gall stone carriers than a material with opposite age distribution. We can therefore only consider the materials in which the percentage of gall stone is given for different age groups and sexes. Tables 3 and



Table 3. *Distribution of gall stone in different year groups, among men and women. Autopsy materials from the literature.*

| Age,<br>years | SCHLOTH 1886                     |                              |                      |                                  |                              |                      | PETERS 1890                      |                              |                      |                                  |                              |                      | SCHEEL 1911                      |                              |                      |                                  |                              |                      |
|---------------|----------------------------------|------------------------------|----------------------|----------------------------------|------------------------------|----------------------|----------------------------------|------------------------------|----------------------|----------------------------------|------------------------------|----------------------|----------------------------------|------------------------------|----------------------|----------------------------------|------------------------------|----------------------|
|               | Men                              |                              |                      | Women                            |                              |                      | Men                              |                              |                      | Women                            |                              |                      | Men                              |                              |                      | Women                            |                              |                      |
|               | Number<br>of au-<br>top-<br>sies | Number<br>of gall-<br>stones | %<br>gall-<br>stones | Number<br>of au-<br>top-<br>sies | Number<br>of gall-<br>stones | %<br>gall-<br>stones | Number<br>of au-<br>top-<br>sies | Number<br>of gall-<br>stones | %<br>gall-<br>stones | Number<br>of au-<br>top-<br>sies | Number<br>of gall-<br>stones | %<br>gall-<br>stones | Number<br>of au-<br>top-<br>sies | Number<br>of gall-<br>stones | %<br>gall-<br>stones | Number<br>of au-<br>top-<br>sies | Number<br>of gall-<br>stones | %<br>gall-<br>stones |
| 0-20          | 676                              | —                            | —                    | 528                              | —                            | —                    | —                                | —                            | —                    | —                                | —                            | —                    | —                                | —                            | —                    | —                                | —                            | —                    |
| 20-30         | 355                              | 4                            | 1,1                  | 201                              | 23                           | 11,4                 | 374                              | 1                            | 0,3                  | 269                              | 3                            | 1,1                  | 137                              | —                            | —                    | 128                              | 7                            | 5,5                  |
| 30-40         | 393                              | 13                           | 3,3                  | 244                              | 20                           | 8,2                  | 411                              | 5                            | 1,2                  | 238                              | 16                           | 6,7                  | 291                              | 10                           | 3,4                  | 157                              | 17                           | 10,8                 |
| 40-50         | 387                              | 21                           | 5,4                  | 243                              | 25                           | 10,3                 | 367                              | 9                            | 2,5                  | 196                              | 16                           | 8,2                  | 249                              | 24                           | 9,6                  | 207                              | 29                           | 14,0                 |
| 50-60         | 364                              | 28                           | 7,7                  | 237                              | 41                           | 17,3                 | 297                              | 8                            | 2,7                  | 163                              | 24                           | 14,7                 | 384                              | 37                           | 9,6                  | 176                              | 44                           | 25,0                 |
| 60-70         | 318                              | 28                           | 8,8                  | 209                              | 42                           | 20,1                 | 237                              | 19                           | 8,0                  | 150                              | 18                           | 12,0                 | 260                              | 34                           | 13,1                 | 189                              | 55                           | 29,1                 |
| 70-80         | 95                               | 19                           | 20,0                 | 147                              | 42                           | 28,6                 | 112                              | 10                           | 8,9                  | 126                              | 21                           | 16,7                 | 219                              | 60                           | 27,4                 | 256                              | 89                           | 34,8                 |
| 80-∞          | 18                               | 1                            | 5,6                  | 52                               | 19                           | 36,5                 | 20                               | 3                            | 15,0                 | 35                               | 6                            | 17,1                 |                                  | 1540                         | 10,71                | 1113                             | 241                          | 21,65                |
| 0-∞           | 2606                             | 114                          | 4,37                 | 1861                             | 212                          | 11,39                | 1818                             | 55                           | 3,03                 | 1177                             | 104                          | 8,84                 | —                                | 165                          | —                    | —                                | —                            | —                    |

Table 4. *Distribution of gall stone in different year groups, among men and women. Autopsy materials from the literature and the author's own material.*

| Age, years | MITCHELL 1918       |                       |               |                     |                       |               | LUDLOW 1937         |                       |               |                     |                       |               | The author          |                       |               |                     |                       |               |
|------------|---------------------|-----------------------|---------------|---------------------|-----------------------|---------------|---------------------|-----------------------|---------------|---------------------|-----------------------|---------------|---------------------|-----------------------|---------------|---------------------|-----------------------|---------------|
|            | Men                 |                       |               | Women               |                       |               | Men                 |                       |               | Women               |                       |               | Men                 |                       |               | Women               |                       |               |
|            | Number of autopsies | Number of gall-stones | % gall-stones | Number of autopsies | Number of gall-stones | % gall-stones | Number of autopsies | Number of gall-stones | % gall-stones | Number of autopsies | Number of gall-stones | % gall-stones | Number of autopsies | Number of gall-stones | % gall-stones | Number of autopsies | Number of gall-stones | % gall-stones |
| 0-20       | 113                 | 2                     | 1.8           | 41                  | 1                     | 2.4           | 551                 | 1                     | 0.2           | 399                 | 1                     | 0.3           | 333                 | —                     | —             | 286                 | 1                     | 0.3           |
| 20-30      | 274                 | 2                     | 0.7           | 68                  | 3                     | 4.4           | 238                 | 6                     | 2.5           | 183                 | 9                     | 4.9           | 138                 | —                     | —             | 146                 | 3                     | 2.1           |
| 30-40      | 326                 | 3                     | 0.9           | 62                  | 6                     | 9.7           | 375                 | 9                     | 2.4           | 257                 | 19                    | 7.4           | 128                 | 1                     | 0.8           | 131                 | 12                    | 9.2           |
| 40-50      | 301                 | 4                     | 1.3           | 42                  | 3                     | 7.1           | 492                 | 31                    | 6.3           | 228                 | 38                    | 16.7          | 152                 | 5                     | 3.3           | 174                 | 21                    | 12.1          |
| 50-60      | 131                 | 4                     | 3.1           | 18                  | 3                     | 16.7          | 394                 | 42                    | 10.7          | 168                 | 38                    | 22.6          | 274                 | 15                    | 5.5           | 203                 | 47                    | 23.2          |
| 60-70      | 71                  | 13                    | 18.3          | 13                  | 2                     | 15.4          | 232                 | 35                    | 15.1          | 105                 | 26                    | 24.8          | 347                 | 24                    | 6.9           | 262                 | 75                    | 28.6          |
| 70-80      | 6                   | 1                     | 16.7          | 3                   | 2                     | 66.7          | 102                 | 14                    | 13.7          | 41                  | 11                    | 26.8          | 299                 | 35                    | 11.7          | 93                  | 79                    | 29.4          |
| 80-∞       | 3                   | 1                     | 33.3          | 1                   | —                     | —             | 8                   | —                     | —             | 6                   | 3                     | 50.0          | 92                  | 17                    | 18.5          | —                   | 31                    | 33.3          |
| 0-∞        | 1225                | 30                    | 2.45          | 248                 | 20                    | 8.06          | 2392                | 138                   | 5.77          | 1387                | 145                   | 10.45         | 1763                | 97                    | 5.50          | 1564                | 269                   | 17.20         |

4 show a number of such investigations made by different authors and referring to different periods. The older materials ought to correspond most closely to the actual state of things, as they include at most a few cases in which gall stones were removed during life and consequently were not found in the post-mortem examination, although they had been present earlier. The material presented by MITCHELL (1918) is obtained from medico-legal autopsies, the other materials are hospital cases.

The different materials show that the frequency of gall stone increases with age. In women, the increase is more rapid after the age of 30, in men a more obvious increase is observed at the ages of 40—50 and over. For all age groups, the frequency is lower for men than for women.

Our material was obtained from the Pathological Institution in Uppsala. We have discussed above, in chapter 2, the composition of the material and pointed out that we have reason to expect that the figures for the frequency of gall stone obtainable in this material, do not deviate too much from those referring to the population to which the material belongs. The figures for the frequency of gall stones which we have obtained on the basis of the material, tally very well with the figures given above, quoted from materials previously published, and also with MITCHELL's figures which were obtained in a material largely made up of deaths by accident.

The material is given in table 4. In our material the frequency figures are of approximately the same order of magnitude as those referring to the materials quoted above. In men, the gall stone frequency begins to increase at the age of 30 in order later to rise continuously. In women, the increase sets in a decade sooner and is more rapid. Up to the age of 70, the figure for women is 3—4 times higher than the one applying to men; after the age of 70, it is double.

The frequency of gall stone increasing with increasing age, also reveals itself by the fact that for men between 20 and 50 it is 1.4, and for men over 50, it is 9.0. The difference is statistically significant (diff. =  $7.6 \pm 1.1$ ). For women, it is 8.0 between 20 and 50 years of age, and 28.1 over 50. The difference is statistically significant (diff. =  $20.1 \pm 2.0$ ).

The difference in the frequencies of gall stone for the different sexes is also revealed in the fact that, for men between the ages

of 20—50 it is 1.4, while for women in the same age group, it is 8.0. The difference is statistically significant (diff. =  $6.6 \pm 1.4$ ). For men over 50, it is 9.0, for women in the same age group, it is 28.1 per cent. The difference is statistically significant (diff. =  $19.1 \pm 1.8$ ).

In our material there is only one case of gall stone in persons under the age of 20 (in a 7-month-old girl). That gall stones may be present at ages under 20, is evidenced by data in the literature. ECKHARDT, for instance, in 1933, reported on a case of gall stone in a child of  $3\frac{1}{2}$  months. POTTER (1928) collected from the literature 140 cases with gall stone at an early age. In 12 cases gall stone had been found in new-born children, in 4 cases in children under the age of 1 year, in 5 cases in children between the ages of 1 and 5, and in 19 cases in children of 5—15 years of age. The other cases were children or infants whose ages were not specified. We have also in our clinical material 3 cases operated on in which gall stones were present in persons under the age of 20.

As the frequency of gall stone continuously increases with increasing age, we must assume that gall stones are formed during the whole lifetime. This means that during the whole life there exists a risk of developing gall stone. It is not possible, however, directly to obtain the magnitude of this risk on the basis of the materials published. An increase in the frequency of gall stone may be an expression of a risk of developing gall stone which is equally great, or increases, during the whole lifetime, but may equally well be due to a risk *decreasing* with age.

In order to obtain an idea of the magnitude and distribution of the risk of developing gall stone we have to calculate the risk of gall stone formation for each age group. This may be done by subtracting the figure for the frequency of gall stone in one age group from the corresponding figure for the immediately higher age group. We have done this in our material, and the risk figures obtained are given in table 5. The figures refer to 100,000 individuals in each age group and are calculated as an annual risk (that is to say the figures given above are multiplied by 100). The age groups in table 4 comprise 20—29 years, 30—39 years, and so forth. This means that the figure given for the age groups refers approximately to the ages of 25 years, 35 years, and so on. For younger ages it is too high, for more advanced ages it is too low.



Table 5. *Annual risk of developing gall stone in a population of 100 000 in each year group. Calculated from autopsy material.*

| Age, years | Men | Women | Both sexes |
|------------|-----|-------|------------|
| 15—24      | —   | 205   | 106        |
| 25—34      | 78  | 711   | 396        |
| 35—44      | 251 | 291   | 296        |
| 45—54      | 218 | 1108  | 502        |
| 55—64      | 144 | 547   | 326        |
| 65—74      | 479 | 74    | 381        |
| 75—84      | 574 | 512   | 594        |

When we subtract the risk figure for one age group from the figure for another age group, this means that we subtract for instance the figure for 25 years on an average from the one for 35 years on an average. The table obtained in this way consequently must refer to the ages of 25—34 years, 35—44 years, and so forth.

The risk of contracting gall stone is represented graphically in curves (see figs 3 and 4), which show the risk represented in the form of a logarithmic curve. The characteristic feature of such a curve is that the distances on the ordinate are plotted on a logarithmic scale. On account of this, a multiplication or division of an arbitrary value on the ordinate by a given factor will always be marked by an equally long distance on the ordinate. For instance, the distance between 25 and  $4 \times 25 = 100$  is the same as that between 100 and  $4 \times 100 = 400$ . In the curves shown in figs. 3 and 4 a rise in the curve of 13.5 mm. corresponds to a doubling of the value of the ordinate.

The figures we have obtained for the risk of developing gall stone show that the risk of developing gall stone rapidly increases for men from the age of 25—34 years to the age of 35—44 years, then decreases up to the age of 55—64, in order to increase again, this time more than earlier. For women, the risk increases from the age of 15—24, tho the age of 25—34, decreases for the next age group in order to increase again, attaining its highest value for the age of 45—54 years. Then the risk decreases with increasing age in order to increase again for ages over 75.

We thus find that the annual risk of developing gall stone has a maximum at an age between 35 and 44 years in men, and at an age between 45 and 54 years in women. It then decreases in order

to increase again after the age of 65 in men, and after the age of 75 in women. Expressed in per cent, the annual risk for women between 25 and 34 years is 0.7 per cent, between 35 and 44 it is 0.3 per cent, between 45 and 54 1.1 per cent, and between 55 and 64 0.5 per cent. In the senium, over the age of 75, it is 0.5 per cent. At these ages the risk for women is lower than the risk for men. For men the risk is considerably lower. It amounts to 0.3 per cent between 35 and 44 years, then decreases and only in the senium attains the value of 0.6 per cent.

The risk figures given must be considered as approximate. They nevertheless illustrate the situation, showing *that the annual risk of developing gall stone at the ages over 25—30 is comparatively great both in men and, especially, in women, that the risk presents certain variations for the different age groups and that the risk is also present in the highest age groups, in which it even reveals a tendency to increase.*

## **2. The risk of contracting gall stone disease from the point of view of the population.**

Attempts have been made to get an idea of the frequency of gall stone disease by examining clinical materials with regard to the ages at which the patients were admitted for treatment. In table 6 a number of fairly large such materials are brought together. The views on the frequency of the disease which have been considered to be justified on the basis of such materials amount to this: in men, the disease occurs chiefly between the ages of 30—60, and in women, in most cases between 20—60. The disease is less frequent at more advanced ages. The figures for the occurrence of the disease obtained in this manner have further been compared with the figures obtained for the occurrence of gall stone in autopsy materials. As in such materials, the frequency of gall stone increases with increasing age, the result of the comparison was that, for ages up to 40—50 years, a correspondence was found between gall stone carriers and gall stone sufferers, whereas for more advanced ages, the frequency of gall stone sufferers decreases in spite of the increasing frequency of gall stone carriers. No attempt, however, has been made to carry out a more thorough statistical investigation on these points. As a matter of fact, it is not possible directly to compare figures from an autopsy material with the frequency of the disease in a clinical material, because the figures in the former case only represent the



frequency at a given moment in a population, and in the latter case represent the frequency of the disease over a given period in a material.

If we want to obtain an idea of the frequency with which a disease occurs in different age groups and sexes, we have to relate the number of diseased persons in each age group to the population to which the material belongs, and for the following reasons. The fact that the greatest percentage of diseased persons is to be found in one age group need not imply that the risk of having the disease is greatest in that age group. The explanation may be that this age group is comparatively well represented in the population. As the number of living persons in each age group decreases continuously towards a more advanced age, it might happen that the number of diseased persons decreases towards a more advanced age in spite of the fact that the risk of having the disease increases with age.

The materials employed in such investigations are also open to certain objections. A material covering only patients operated on, or only patients not operated on, needs must yield figures which are not wholly accordant with the actual state of things. In materials comprising cases operated on, young and middle-aged persons are chiefly included, in materials of cases not operated on we may expect to find a comparatively large number of elderly persons who just on account of their age were not operated on. The same difference in age distribution between the cases operated on and the cases not operated on is also present in our own clinical material. Only materials comprising both patients operated on and patients not operated on, allow of definite conclusions as to the frequency of the disease. No comprehensive such material has as yet been published.

The material at our disposal, however, may be considered as fairly satisfactory. It is made up of the clinical cases of gall stone disease which were treated in the surgical department of the Academical Hospital in Uppsala during the years 1922—1935. We have pointed out above (p. 36) that some patients who were admitted to the medical department of the hospital for gall stone disease, were not transferred to, or later admitted to, its surgical department. As the number of these cases, which accordingly are not included in our material, is comparatively small, we are justified in looking upon our clinical material as fairly representative of the cases of gall stone disease which have come to the hospital for treatment.



The number of those who come to the hospital for treatment of their gall stone disease has increased with practically every year during the period covered by the material. We shall return below to these problems (see p. 51).

The population to which the hospital material refers, is the population of the province and city of Uppsala. We may take it that the majority of those among the inhabitants of the town who contract gall stone disease and are in need of treatment in a hospital, are treated in the Academical Hospital. Some patients have come to another hospital for treatment, in the town or elsewhere. The number of these persons, however, cannot be so large as to affect the result of the investigation to any considerable degree. Most of the patients from the province of Uppsala also come to the Academical Hospital for treatment. Some patients have been treated in other hospitals in the province, but as the latter are comparatively small, not many patients should be lacking in our material for this reason.

Our clinical material only comprises such cases of gall stone disease as have come to hospital for treatment. It is fairly usual that mild cases with infrequent and above all mild attacks do not come to hospital but are treated in their homes by medical practitioners. It even happens at times that patients with very mild attacks do not subject themselves to medical treatment at all. It is impossible to determine the number of such cases. We have reason to assume, however, that the majority of the cases with fairly advanced symptoms come to the hospital for treatment. For practical reasons we have to restrict our investigation into the risk factors inherent in gall stone disease to comprise only such cases as have come to the hospital for treatment. As regards the cases from the city of Uppsala, we may also assume that the number of cases which have not come to the hospital for treatment, is comparatively small. It might on the other hand be imagined that patients living in the country, at a considerable distance from the hospital, are treated in their homes by medical practitioners to a larger extent than patients in the town, particularly if the disease is of a comparatively mild type.

We may thus maintain that the part of the material which refers to the city of Uppsala, comprises the majority of those suffering from gall stone disease, and that the part of the material which refers to the province of Uppsala (exclusive of the city of Uppsala), although it does not include as great a percentage of those actually suffering

from gall stone disease as does the material from the town, yet no doubt comprises the majority of such cases. Among the clinical cases included in the material, the cases operated on may be looked upon as quite clear cases of gall stone disease. It is probable that among the cases not operated on, there are some which have had clinical symptoms of gall stone disease but which have not had stones. The number of these cases, however, should be comparatively small (cf. p. 36). The figures to be obtained from our material as to the risk of contracting gall stone disease, for reasons suggested above have to be looked upon as minimum figures. As, further, the material from a statistical point of view is comparatively small, the data must be considered as more or less approximate.

As mentioned above, the clinical material has increased continuously during the years in which it was collected. In table 7 the material is given, grouped in the periods 1922—1927, 1928—1931, and 1932—1935. The material is related to the population to which it belongs, i. e. the population of the province of Uppsala. The

Table 7. *Annual number of persons treated for gall stone disease during the years 1922—1927, 1928—1931 and 1932—1935 among 100.000 in each age group of the average population in the province of Uppsala.*

| Age at first stay in hospital | 1922—1927 |       |            | 1928—1931 |       |            | 1932—1935 |       |            |
|-------------------------------|-----------|-------|------------|-----------|-------|------------|-----------|-------|------------|
|                               | Men       | Women | Both sexes | Men       | Women | Both sexes | Men       | Women | Both sexes |
| 10—14                         | —         | —     | —          | —         | —     | —          | —         | 4     | 2          |
| 15—19                         | 3         | 6     | 4          | —         | 8     | 4          | —         | —     | —          |
| 20—24                         | 3         | 35    | 18         | 4         | 30    | 17         | 4         | 35    | 19         |
| 25—29                         | 6         | 98    | 52         | 9         | 68    | 39         | 9         | 98    | 53         |
| 30—34                         | 7         | 65    | 37         | 20        | 86    | 53         | 24        | 102   | 64         |
| 35—39                         | 15        | 105   | 62         | 32        | 178   | 107        | 62        | 150   | 107        |
| 40—44                         | 26        | 121   | 76         | 37        | 125   | 83         | 41        | 154   | 100        |
| 45—49                         | 34        | 99    | 68         | 46        | 205   | 128        | 26        | 205   | 120        |
| 50—54                         | 38        | 154   | 99         | 85        | 222   | 157        | 51        | 227   | 143        |
| 55—59                         | 48        | 128   | 91         | 110       | 163   | 138        | 52        | 346   | 207        |
| 60—64                         | 20        | 183   | 107        | 59        | 213   | 142        | 79        | 240   | 165        |
| 65—69                         | 100       | 115   | 108        | 75        | 222   | 156        | 153       | 323   | 245        |
| 70—74                         | 20        | 100   | 63         | 82        | 142   | 114        | 122       | 215   | 172        |
| 75—79                         | —         | 35    | 19         | 105       | 120   | 113        | 61        | 84    | 73         |
| 80—84                         | —         | 63    | 35         | —         | 65    | 34         | 147       | 211   | 182        |
| 85—89                         | —         | —     | —          | —         | —     | —          | —         | 73    | 42         |
| 10—89                         | 17        | 78    | 48         | 32        | 108   | 71         | 35        | 133   | 85         |

population figures employed refer to the censuses of 1920, 1930 och 1935. The annual number of treated patients is calculated on 100 000 of the average population in each age group.

If we compare the figures for both sexes from the different periods and the curves to be obtained from those figures (see fig. 2), we

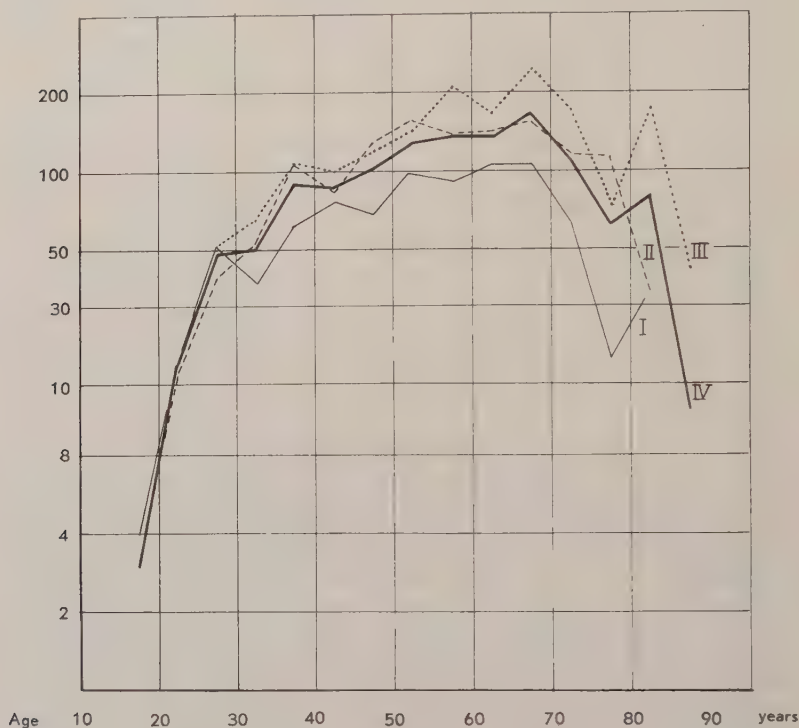


Fig. 2. Annual number of cases treated for gall stone disease calculated on 100.000 inhabitants in each age group during the years 1922—1927, 1928—1931, 1932—1935 and 1922—1935 (see table 7 and 8, both sexes).  
I = 1922—1927 II = 1928—1931 III = 1932—1935 IV = 1922—1935

find that the increase in the material is remarkably homogeneous in the different age groups. The curves are practically parallel. The increase may be due to several causes. In recent years the methods of diagnosing the disease (particularly by cholecystographic examination) have been improved. An increase of the material due to the diagnosis being made in a larger number of cases, should, as is the case in our material, bring about a proportionally similar increase in different age groups. The patients may in recent years

have come to treatment for their disease to a larger extent than previously. It is naturally impossible to decide what an increase of the material, caused in this way, would actually be like. We might expect a more pronounced increase in the higher age groups. Elderly people were formerly in many cases afraid of being admitted to a hospital, but it would seem as if the »dread of the hospital» has diminished in recent years. It might also be expected that the youngest age groups would also show an increase because young people might come to the hospital for treatment in an earlier stage of the disease. Factors of this kind should give a higher curve, which should take a slightly different course from the lower curve for the earlier period. However, no differences of this kind between the curves could be found. It may well be that the factors we have discussed above have not had an influence strong enough to cause obvious differences, but we cannot on this account exclude the possibility that a general increase in the material due to an increased popularity of the hospitals may exist. Finally, the increase in the material might be thought to be due to the frequency of the disease having increased. There is no proof in support of this assumption.

It seems to us probable that the increased frequency found in our material may be explained principally by improved diagnostical methods but also by the patients having come to the hospital for treatment to a larger extent than previously. On the basis of our material it is not possible to decide whether an actual increase in the frequency of the disease has taken place.

The increase of the material is fairly homogeneous in all age groups. When we want to obtain an idea of the risk of being taken ill in different age groups, we are therefore justified in bringing together the material for the different periods and analyse it in its entirety.

In table 8 the total material is given. In this table it is not grouped in town and country. The table shows that the frequency of gall stone sufferers increases continuously with age, both for men and women. The figures for men keep at a lower level than those for women. In this table as in tables 9, 12 and 13 the figures for ages over 70 are less reliable than for other ages, as the clinical material for these age groups is fairly small, and, further, the oldest cases of gall stone disease no doubt come to the hospital for treatment to a comparatively smaller extent than those who are younger.



Table 8. *Annual number of persons treated for gall stone disease during the years 1922—1935 among 100.000 in each age group of the average population in the province of Uppsala.*

| Age at first<br>stay in hospital | 1922 — 1935 |       |            |
|----------------------------------|-------------|-------|------------|
|                                  | Men         | Women | Both sexes |
| 10—14                            | —           | 1     | 1          |
| 15—19                            | 1           | 5     | 3          |
| 20—24                            | 4           | 34    | 18         |
| 25—29                            | 8           | 89    | 48         |
| 30—34                            | 16          | 82    | 49         |
| 35—39                            | 34          | 139   | 88         |
| 40—44                            | 33          | 132   | 85         |
| 45—49                            | 35          | 161   | 101        |
| 50—54                            | 55          | 194   | 128        |
| 55—59                            | 65          | 197   | 136        |
| 60—64                            | 48          | 208   | 134        |
| 65—69                            | 109         | 209   | 164        |
| 70—74                            | 69          | 146   | 111        |
| 75—79                            | 48          | 73    | 62         |
| 80—84                            | 43          | 105   | 78         |
| 85—89                            | —           | 20    | 12         |
| 10—89                            | 27          | 103   | 66         |

The figures on the frequency of gall stone disease to be obtained on the basis of our material, however, cannot be taken as indicative of the *risk* of contracting gall stone disease. The figures given are only figures showing how often we may expect in a population to find persons suffering from gall stone disease who for the first time *come to hospital to be treated* for their disease.

As the relative number of those who come to treatment for their disease increases with increasing age in the material, and as, further, we have reason to expect that the time interval between the onset of the disease and the treatment in hospital does not increase with rising age (but, on the other hand, rather decreases) for different age groups (see below chapt. 7), we may expect the risk of contracting gall stone disease to be present during the whole lifetime. This risk may be of the same order of magnitude during the whole life. It may be of varying magnitude in different age groups, or it may decrease with age.

In order to get an idea of the *risk of falling ill* with gall stone disease, the material has to be related to the age at which the patient

was taken ill. This can only be done by trying to record the age at which the first attack of the disease occurred in each case, on the basis of data available in the diaries. Another alternative naturally would be only to include those cases in the clinical material who have come to the hospital for treatment during the first attack of the disease. In the material at our disposal, however, too small a number of such cases are included.

We have proceeded as follows.

On the basis of the hospital diaries available we recorded for each case in the material the age at which the patient developed the first signs of his disease. In the cases in which the patient came to treatment after the first onset of the disease, we only paid regard to the time of the first attack of pain which in most cases was recorded by the patient with great accuracy. In some cases the attacks of pain are absent, or not very intense: the disease reveals itself by more chronic discomforts, usually of a dyspeptic type. In the cases in which attacks of pain appeared in combination with such more chronic discomforts, we dated the disease from the time of the first attack of pain. As such discomforts are not very typical it is as a rule impossible to determine the exact time when they first appeared; we therefore did not include the cases in which attacks of pain were absent. The cases in our material which for this reason were not included, are 4 in number. Further, in 4 cases, exact data as to the first attack of pain are lacking; it is only stated that the patient has had attacks »for several years» or words to that effect.

The material was further divided into two groups, one comprising the cases from the city of Uppsala, the other the cases from the province of Uppsala (exclusive of the city of Uppsala).

Table 9 gives the calculated risk figures.

We shall first consider the risk figures relating to the material from the city of Uppsala (see figs. 3 and 4). The material is subdivided into 5-year groups, and the risk is calculated as the annual risk applying to a population of 100,000 individuals. For men, the risk of falling ill with gall stone disease begins to reveal itself in the group of 15—19 years; it is then comparatively small. For the next age group it is greater in order to give a lower value again for the age group of 25—29. These variations between the age groups are not statistically significant. The risk of falling ill subsequently increases for each 5-year period, until, for the age

Table 9. *Annual risk of being taken ill with gall stone disease among 100.000 of the average population, calculated for the city of Uppsala, for the province of Uppsala (excl. of city of Uppsala) and for the entire province of Uppsala.*

| Age at time of first attack | City of Uppsala |       |            | Province of Uppsala (excl. of city of Uppsala) |       |            | Entire province of Uppsala |       |            |
|-----------------------------|-----------------|-------|------------|------------------------------------------------|-------|------------|----------------------------|-------|------------|
|                             | Men             | Women | Both sexes | Men                                            | Women | Both sexes | Men                        | Women | Both sexes |
| 10—14                       | —               | 14    | 7          | —                                              | 1     | 1          | —                          | 3     | 2          |
| 15—19                       | 6               | 24    | 16         | 1                                              | 20    | 10         | 2                          | 21    | 12         |
| 20—24                       | 22              | 90    | 61         | 11                                             | 66    | 41         | 14                         | 73    | 47         |
| 25—29                       | 5               | 127   | 74         | 10                                             | 102   | 53         | 9                          | 110   | 59         |
| 30—34                       | 25              | 135   | 86         | 28                                             | 95    | 61         | 27                         | 106   | 68         |
| 35—39                       | 60              | 141   | 105        | 25                                             | 163   | 94         | 33                         | 157   | 97         |
| 40—44                       | 70              | 125   | 101        | 32                                             | 117   | 75         | 40                         | 119   | 82         |
| 45—49                       | 79              | 183   | 139        | 28                                             | 148   | 89         | 39                         | 158   | 101        |
| 50—54                       | 82              | 193   | 146        | 36                                             | 154   | 96         | 46                         | 164   | 108        |
| 55—59                       | 102             | 132   | 120        | 37                                             | 188   | 114        | 50                         | 173   | 116        |
| 60—64                       | 106             | 146   | 131        | 28                                             | 147   | 89         | 42                         | 147   | 98         |
| 65—69                       | 171             | 159   | 163        | 75                                             | 129   | 103        | 93                         | 137   | 117        |
| 70—74                       | 115             | 143   | 133        | 54                                             | 106   | 81         | 65                         | 115   | 92         |
| 75—79                       | 34              | 132   | 97         | 29                                             | 39    | 34         | 30                         | 63    | 48         |
| 80—84                       | 124             | 108   | 114        | 26                                             | 69    | 49         | 43                         | 79    | 63         |
| 85—89                       | —               | —     | —          | —                                              | 27    | 15         | —                          | 20    | 12         |
| 10—89                       | 48              | 118   | 88         | 22                                             | 96    | 59         | 27                         | 102   | 66         |

groups of 40—44 and 45—49 it is approximately identical, then showing a moderate increase for the following age groups. The risk of being taken ill is greatest for the highest age group (65—69 years). For women, we are able, on the basis of our material, to observe a risk of being taken ill even for the group of 10—14 years. The risk then increases rapidly up to the age group of 25—29, shows a slight decrease for the age of 40—44 years, followed by an increase for the group of 45—49 years. The risk of falling ill is, for the group of 50—54 years, about the same as for the preceding age group but shows a moderate decrease for the next 5-year period. For the subsequent age groups the risk keeps on about the same level as before.

The risk figures referring to that part of the material which was obtained in the province of Uppsala (exclusive of the city of Uppsala) are, as regards women, practically identical with the figures given

above. The curve takes on the whole a similar course: one maximum falls at the age between 35 and 39 years, and another between 55 and 59 years. Between these maxima, the curve declines somewhat, as also after the age of 65. The risk figures for men show certain deviations from the figures given above, which latter refer to the population of the city of Uppsala. The curves take a parallel course to begin with; after a rapid increase in the risk figures from the age group of 15—19 to the next age group, the risk decreases for the subsequent group, 25—29 years. Then the risk increases and for the age group of 30—34 it is equally great with the corresponding figure for the population of the city of Uppsala. In the following age groups, the risk figures show a moderate increase and throughout keep on a lower level than the corresponding figures for the population of the city of Uppsala. The question arises why the figures for the risk of falling ill are smaller for men over the age of 35 in the countryside round Uppsala than in the town itself. It is hardly probable that the actual risk of falling ill is smaller. In that case we should expect both that a similar variation would occur in the curve representing the risk of falling ill for women, and that the deviations in the risk curve for the men would appear in all age groups and not only at certain ages. The explanation is probably that the men who are taken ill after the age of 35 come to the hospital for treatment to a smaller extent than men who are taken ill at a younger age and than women. Why this should be so, we are not prepared to explain, however.

As pointed out above, the risk figures to be obtained in our material must be looked upon as approximate. Nevertheless, they throw quite a different light on the situation as compared to the views formerly held. *The risk of contracting gall stone disease increases rapidly up to the age of 25, both for men and women. For women, the risk then shows a slight increase with a maximum at the age of 50. For men, the risk increases during the whole lifetime from the age of 30.* We may get an idea of the absolute magnitude of the risk by noting that the annual risk of contracting gall stone disease is 0.16 per cent for women at the age of 50.



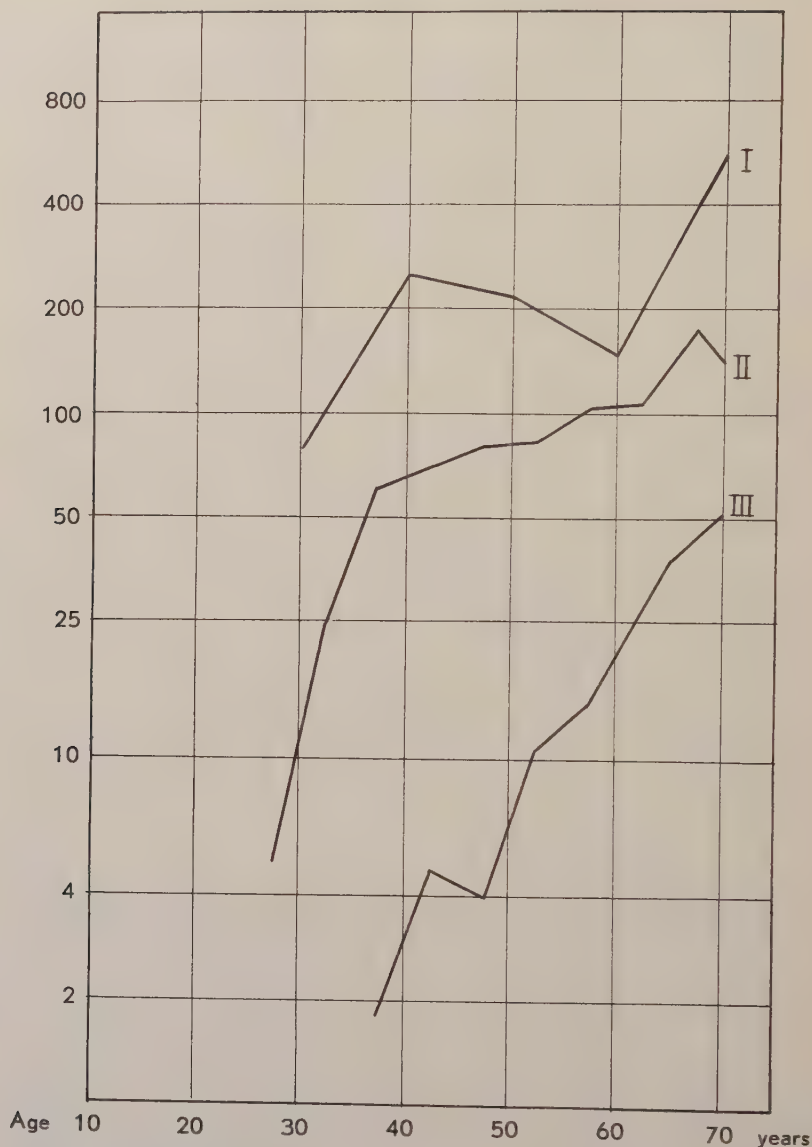


Fig. 3. Curves showing for *men*: I annual risk of developing gall stone (on the basis of autopsy material, see table 12). II annual risk of being taken ill with gall stone disease (on the basis of clinical material from city of Uppsala, see table 9), III annual risk of dying from gall stone disease (on the basis of material from the official statistics, see table 11).

The vertical scale represents number per 100000. The horizontal scale gives the age.

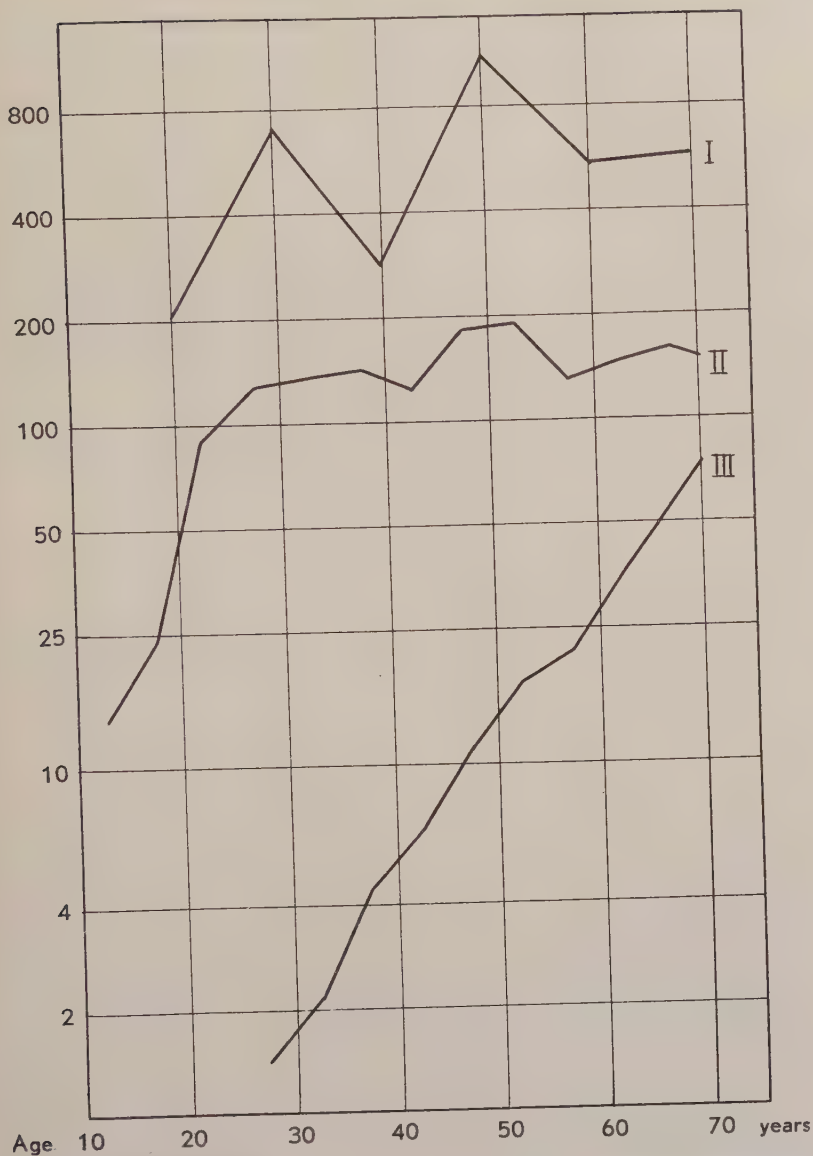


Fig. 4. Curves showing for *women*: I annual risk of developing gall stone (on the basis of autopsy material, see table 12), II annual risk of being taken ill with gall stone disease (on the basis of clinical material from city of Uppsala, see table 9), III annual risk of dying from gall stone disease (on the basis of material from the official statistics, see table 11).

The vertical scale represents number per 100000. The horizontal scale gives the age.

### 3. The risk of dying from gall stone disease from the point of view of the population.

The material underlying this risk examination was obtained from the official statistics of Sweden. It comprises all deaths from gall stone and inflammation of the gall bladder in Swedish towns during the years 1931—1935, in all 1130 cases, 344 men and 786 women. In table 10 the absolute figures for deaths from gall stone disease

Table 10. *Deaths from gall stone disease in the Swedish towns during the years 1931—1935 (material from the official statistics of Sweden).*

| Age,<br>years | Total number<br>of deaths |       | Deaths from gall stone disease among these |       |      |       |
|---------------|---------------------------|-------|--------------------------------------------|-------|------|-------|
|               |                           |       | Number of cases                            |       | ‰    |       |
|               | Men                       | Women | Men                                        | Women | Men  | Women |
| 0—5           | 4152                      | 3049  | —                                          | —     | —    | —     |
| 5—10          | 581                       | 447   | —                                          | —     | —    | —     |
| 10—15         | 534                       | 415   | —                                          | —     | —    | —     |
| 15—20         | 997                       | 986   | —                                          | —     | —    | —     |
| 20—25         | 1551                      | 1729  | —                                          | 5     | —    | 2,9   |
| 25—30         | 1575                      | 1684  | 4                                          | 8     | 2,5  | 4,8   |
| 30—35         | 1545                      | 1623  | 3                                          | 11    | 1,9  | 6,8   |
| 35—40         | 1676                      | 1615  | 7                                          | 20    | 4,2  | 12,4  |
| 40—45         | 2052                      | 1810  | 17                                         | 27    | 8,3  | 14,9  |
| 45—50         | 2720                      | 2300  | 13                                         | 41    | 4,8  | 17,8  |
| 50—55         | 3322                      | 2722  | 29                                         | 57    | 8,7  | 20,9  |
| 55—60         | 3836                      | 3281  | 32                                         | 58    | 8,3  | 17,7  |
| 60—70         | 9589                      | 9930  | 109                                        | 187   | 11,4 | 18,8  |
| 70—           | 18340                     | 28243 | 130                                        | 372   | 7,1  | 13,2  |
| Total         | 52470                     | 59834 | 344                                        | 786   | 6,6  | 13,1  |

in different age groups are given and compared with the total number of deaths in the corresponding age groups in Swedish towns. The table shows that the relative number of reported deaths from gall stone disease increases with increasing age up to the age of 55 in order subsequently to decrease somewhat.

The risk of dying from gall stone disease is shown in table 11 and in figs. 3 and 4. The deaths from gall stone disease are related to the number of living persons in the different age groups during the 5-year period 1931—1935. In early years the risk of dying from this disease is fairly small but it increases rapidly with increasing age. Roughly speaking, the risk is doubled for each 5-year period after the age of 35. The risk figure for ages over 70 is perhaps not

altogether reliable, as the population in this age group is comparatively small; no doubt, however, this risk figure is fairly high and greater than the one applying to the previous age group.

For men in all age groups, the risk of dying from the disease is, from the point of view of the population, smaller than for women, but otherwise it shows the same increase with rising age with the exception of the group of 45—50 years, at which the risk of dying is smaller than in the previous age group. This may be related to the circumstance that the risk of being taken ill is also smaller for the age group of 45—50 years than for the previous age group. The

Table 11. *Annual risk of dying from gall stone disease among 100.000 inhabitants in towns of Sweden, 1931—1935.*

| Age, years | Men   | Women  | Both sexes |
|------------|-------|--------|------------|
| 20—24      | —     | 0,86   | 0,48       |
| 25—29      | 0,86  | 1,41   | 1,16       |
| 30—34      | 0,71  | 2,19   | 1,51       |
| 35—39      | 1,80  | 4,46   | 3,23       |
| 40—44      | 4,80  | 6,57   | 5,75       |
| 45—49      | 4,07  | 11,11  | 7,84       |
| 50—54      | 10,50 | 17,73  | 14,39      |
| 55—59      | 14,41 | 21,56  | 18,33      |
| 60—69      | 37,24 | 46,47  | 42,59      |
| 70—        | 70,67 | 119,67 | 101,45     |

smaller risk figure for the men no doubt is connected with the fact that men are affected by the disease to a much smaller extent than women. In our clinical material, the relation between men and women thus is 1:4 (the men making up 19,9 per cent). We shall return later to the question as to whether men suffering from gall stone disease run the same death-risk as diseased women, but we may in this connection point out that the death-risk for diseased men does not essentially differ from the one applying to diseased women.

If we represent graphically the risk of dying from gall stone disease incurred by men and women at different ages, we get the curves shown in figs. 3 and 4. The curves show, as is also emphasized in the text, that the risk increases continuously during the whole lifetime and that the risk of dying from the gall stone disease is, roughly speaking, doubled in each 5-year period.



#### 4. The risk of contracting gall stone disease for persons who have gall stone.

In the previous pages we have dealt with the risk of developing gall stone, the risk of contracting gall stone disease, and the risk of dying from gall stone disease. We shall now relate these risks to one another, and begin by examining the risk of contracting gall stone disease for persons who have gall stone.

For this purpose we compare the curve showing the risk of developing gall stone with the one showing the risk of contracting gall stone disease (see figs. 3 and 4). A rise, or fall, in the curve showing the risk of developing gall stone, corresponds to a similar change in the curve showing the risk of falling ill. The changes in the latter curve, however, only reveal themselves somewhat later, as a rule at the point corresponding to the next 5-year period. This indicates that an increased, or decreased, risk of developing gall stone is accompanied by an increased, or decreased, risk of falling ill with gall stone disease within a time of about 5 years.

Under such circumstances we may put the risk figure for developing gall stone in relation to the risk figure for contracting gall stone disease for the same age group and to the figure for the immediately higher age group. In both cases the results are fairly similar: between 15 and 50 per cent in both cases of those who develop gall stone are taken ill with gall stone disease, men as well as women (see table 12). From a statistical point of view our material is fairly small. It is not excluded that larger materials might give a still closer agreement between the risk of developing gall stone and the risk of being taken ill. Similarly, we might expect to obtain more definite data on the time interval between gall stone formation and gall stone disease if we only had a large enough material to enable us to determine accurate risk figures for each one-year age group.

Our material shows that there exists an obvious connection between the risk of developing gall stone and the risk of falling ill with gall stone disease. We have previously mentioned that there is some doubt as to the part played by gall stone in the development of gall stone disease. It has been suggested in the first place that infection of the gall bladder or biliary ducts might be very important to both the formation of gall stone and the development

Table 12. *Comparison between annual risk of developing gall stone and annual risk of being taken ill, a) on the assumption that the disease appears during the same 10-year period as gall stone is formed, b) on the assumption that the disease appears in the subsequent 10-year period. The risks calculated on 100.000 persons in each year group.*

| Age, years | Risk of developing gall stone |       |            | Risk of being taken ill |       |            | Percentage of persons taken ill out of those who develop gall stone in the same 10-year period |       |            | Percentage of persons taken ill out of those who develop gall stone in the subsequent 10-year period |       |            |
|------------|-------------------------------|-------|------------|-------------------------|-------|------------|------------------------------------------------------------------------------------------------|-------|------------|------------------------------------------------------------------------------------------------------|-------|------------|
|            | Men                           | Women | Both sexes | Men                     | Women | Both sexes | Men                                                                                            | Women | Both sexes | Men                                                                                                  | Women | Both sexes |
| 15—24      | —                             | 205   | 106        | 7                       | 47    | 28         | —                                                                                              | 23    | 26         | —                                                                                                    | 53    | 59         |
| 25—34      | 78                            | 711   | 396        | 17                      | 108   | 63         | 22                                                                                             | 15    | 16         | 46                                                                                                   | 20    | 23         |
| 35—44      | 251                           | 291   | 296        | 36                      | 139   | 90         | 14                                                                                             | 48    | 30         | 17                                                                                                   | 55    | 35         |
| 45—54      | 218                           | 1108  | 502        | 42                      | 161   | 104        | 19                                                                                             | 15    | 21         | 22                                                                                                   | 15    | 22         |
| 55—64      | 144                           | 547   | 326        | 47                      | 161   | 108        | 33                                                                                             | 29    | 33         | 56                                                                                                   | 23    | 33         |
| 65—84      | 1053                          | 586   | 975        | 66                      | 108   | 89         | 6                                                                                              | 18    | 9          | 3.                                                                                                   | 11    | 5          |

of gall stone disease. The question then arises as to how frequently gall stone is formed with infection, or without infection, without giving clinical symptoms. We naturally cannot give an answer to this question; we are only able to give an approximate idea of how often gall stone is formed on the basis of the materials at our disposal. We cannot estimate the part played by a possible infection in this connection. In the cases in which we find symptoms of gall stone disease we ask: is it possible to have clinical symptoms of the disease without having gall stone? We have previously pointed out several times that a clinical picture of gall stone disease occasionally occurs in the absence of gall stone, and we have further shown that this clinical picture is comparatively infrequent as compared to the cases of gall stone disease with gall stone. From a practical point of view we consequently have to look upon gall stone as a prerequisite condition for gall stone disease.

We might further ask whether symptoms of gall stone disease may appear without being accompanied by infection of the gall bladder or the biliary ducts. In the majority of cases which present clinical symptoms of gall stone disease but no clear infection of the gall bladder, gall stones are found in the gall bladder or biliary ducts. There are isolated cases, usually without wholly typical symptoms of gall stone disease, in which an apparently normal

gall bladder without stone is found at operation. Such cases (cholecystosis) are etiologically obscure; in a fair number of these cases the symptoms no doubt result from changes in other organs (duodenum, appendix).

If infection is decisive to the development of gall stone disease, we might ask whether infection is more easily developed when stone is present in the gall bladder or not. The clinical picture of gall stone disease appears by far more frequently when gall stone is present. If infection were to develop as easily in the presence of gall stone as in its absence, the explanation must be that infection in the absence of gall stone comparatively oftener takes such a mild course that it does not bring out any clinical symptoms.

Our material does not allow us to take up a definite position as to the question of the part played by infection in gall stone and gall stone disease. We only wanted to mention the questions that ought to be answered in the discussion of this problem.

*The risk of developing gall stone without contracting gall stone disease.* This risk naturally corresponds wholly to the risk of developing gall stone and the risk of contracting gall stone disease. We need only subtract the figure, calculated in per cent, for the risk of contracting the disease (table 12) from 100 in order to obtain the risk of having gall stone without clinical symptoms (innocent gall stone). This risk comprises between 50 and 85 per cent of those who develop gall stone. The figure is of the same order of magnitude for both men and women.

##### **5. The death-risk for persons suffering from gall stone disease.**

We may arrive at an idea of the risk of dying for persons suffering from gall stone disease by relating the risk figures for being taken ill to the figures for the risk of dying from the disease. These latter figures refer to the population in the Swedish towns. We have therefore related them to the risk figures for being taken ill obtained from the population of the city of Uppsala, on the assumption that the risk of dying shows a close relation of time to the risk of being taken ill. The result of the comparison appears in table 13. We find that the risk of dying from the disease shows a continued increase with rising age in the material. For women falling

Table 13. *Comparison between observed annual number of deaths from gall stone disease and expected annual number of persons taken ill in the Swedish towns during the years 1931—1935 (on the assumption that the same risk of being taken ill applies to all Swedish towns as to the city of Uppsala).*

| Age, years | If death is assumed to occur in the same 5-year period as appearance of disease |                                          |                              |                  |                                          |                              | If death is assumed to occur in the subsequent 5-year period to appearance of disease |                                          |                              |                  |                                          |                              |
|------------|---------------------------------------------------------------------------------|------------------------------------------|------------------------------|------------------|------------------------------------------|------------------------------|---------------------------------------------------------------------------------------|------------------------------------------|------------------------------|------------------|------------------------------------------|------------------------------|
|            | Men                                                                             |                                          |                              | Women            |                                          |                              | Men                                                                                   |                                          |                              | Women            |                                          |                              |
|            | Number of deaths                                                                | Calculated number of persons taken ill N | Percentage of deaths among N | Number of deaths | Calculated number of persons taken ill N | Percentage of deaths among N | Number of deaths                                                                      | Calculated number of persons taken ill N | Percentage of deaths among N | Number of deaths | Calculated number of persons taken ill N | Percentage of deaths among N |
| 20—24      | —                                                                               | 20                                       | —                            | 1                | 104                                      | 1                            | 1                                                                                     | 20                                       | 5                            | 2                | 104                                      | 2                            |
| 25—29      | 1                                                                               | 5                                        | 20                           | 2                | 144                                      | 1                            | 1                                                                                     | 5                                        | 20                           | 2                | 144                                      | 1                            |
| 30—34      | 1                                                                               | 21                                       | 5                            | 2                | 136                                      | 2                            | 1                                                                                     | 21                                       | 5                            | 4                | 136                                      | 3                            |
| 35—39      | 1                                                                               | 47                                       | 2                            | 4                | 127                                      | 3                            | 3                                                                                     | 47                                       | 6                            | 5                | 127                                      | 4                            |
| 40—44      | 3                                                                               | 50                                       | 6                            | 5                | 103                                      | 5                            | 3                                                                                     | 50                                       | 6                            | 8                | 103                                      | 8                            |
| 45—49      | 3                                                                               | 51                                       | 6                            | 8                | 135                                      | 6                            | 6                                                                                     | 51                                       | 12                           | 11               | 135                                      | 8                            |
| 50—54      | 6                                                                               | 45                                       | 13                           | 11               | 124                                      | 9                            | 6                                                                                     | 45                                       | 13                           | 12               | 124                                      | 10                           |
| 55—59      | 6                                                                               | 45                                       | 13                           | 12               | 71                                       | 17                           | 11                                                                                    | 45                                       | 24                           | 18               | 71                                       | 25                           |
| 60—69      | 22                                                                              | 80                                       | 28                           | 37               | 123                                      | 30                           | 18                                                                                    | 80                                       | 23                           | 37               | 123                                      | 30                           |
| 20—69      | 43                                                                              | 364                                      | 12                           | 82               | 1067                                     | 8                            | 50                                                                                    | 364                                      | 14                           | 99               | 1067                                     | 9                            |

ill before the age of 35, the risk of dying lies between 1 and 2 per cent. For those falling ill between 35 and 39, the risk increases up to 3 per cent and also increases at subsequent ages. For those falling ill after the age of 54, the risk of dying increases more rapidly. Later, it is almost doubled for each 5-year period, from having previously increased by about 50 per cent. For those falling ill after the age of 70, we lack reliable figures, as the material referring to these ages is too small. The men yield figures corresponding to the ones obtained for the women. For those being taken ill up to the age of 40, the risk of dying is about 3 per cent (the high risk figure for those falling ill at the age of 25—29 is not reliable, as the clinical material for this age group only comprised one person). For those falling ill between the ages of 40 and 50, the risk of dying is doubled, or 6 per cent. It is doubled for those falling ill in the next age group, reaching its maximum for those being taken ill between 60 and 70.



It might be objected that death does not follow immediately on the onset of the disease but only years afterwards. Under such circumstances the risk of dying ought rather to be related to the risk of being taken ill applying to a lower age group. We have related them to the immediately lower age group. The risk of dying between 30 and 34 thus is compared to the risk of falling ill between 25 and 29 (table 13). The figures for the risk of dying obtained in this manner tally rather well with those found in the previous table, as long as we are concerned with persons being taken ill in earlier age groups. We then find for women a very marked increase in the risk of dying for those who are taken ill between 55 and 59 years and later. For this age group, the risk is 2—3 times greater than the one applying to the previous age group. This does not seem very probable. We find a corresponding pronounced increase in risk for men falling ill at the age of 55—59 years. For this age group, the risk is 2 times greater than the one for the previous age group.

We may obtain an idea of what the situation is really like by examining a clinical material (see table 14). We have subdivided our clinical material, comprising cases operated on and cases not operated on, into age groups, corresponding to the first attack of gall stone disease, that is to say to the time when the patient was first taken ill. We have further entered into the table those patients who died from their disease, arranged according to the time elapsed from the onset of the disease to the death. The majority of the deaths occurred in the hospital, in connection with the first stay there (63 cases) or a later stay in hospital (3 cases). Out of the patients treated during the years 1922—1930, those who were discharged from the hospital were re-examined. Of 510 cases, 5 were found to have died from gall stone disease in their homes or in another hospital (they are included in the table). For this reason it is probable that some of those who were treated in the hospital during the years 1931—1935 later died in their homes or in another hospital from their disease. These deaths are thus not included in the material. On the other hand we have to assume that the number of these cases is small, as only 5 out of those treated in previous years died outside the hospital. We may assert that the table gives an illustration of the minimum mortality in the material, and that the figures must be considered as fairly reliable.

Table 14. *Deaths from gall stone disease in the hospital (66 cases) and later on (5 cases). Distribution according to age at first attack and interval between first attack and death.*

| Age at first attack | Men                                     |        |         |         |         |         |            |             |                    |       | Women                                   |        |         |         |         |         |            |             |                    |       |    |
|---------------------|-----------------------------------------|--------|---------|---------|---------|---------|------------|-------------|--------------------|-------|-----------------------------------------|--------|---------|---------|---------|---------|------------|-------------|--------------------|-------|----|
|                     | Interval between first attack and death |        |         |         |         |         |            |             |                    |       | Interval between first attack and death |        |         |         |         |         |            |             |                    |       |    |
|                     | Deaths at first attack                  | 1 year | 2 years | 3 years | 4 years | 5 years | 6-10 years | 11-20 years | More than 20 years | Total | Deaths at first attack                  | 1 year | 2 years | 3 years | 4 years | 5 years | 6-10 years | 11-20 years | More than 20 years | Total |    |
| 20-24               | —                                       | —      | —       | —       | —       | —       | —          | —           | —                  | —     | 1                                       | —      | —       | —       | —       | —       | —          | —           | —                  | 2     | 3  |
| 25-29               | —                                       | —      | —       | —       | —       | —       | —          | —           | —                  | —     | —                                       | —      | —       | —       | —       | —       | —          | —           | 1                  | 1     | 1  |
| 30-34               | —                                       | —      | —       | —       | —       | —       | —          | —           | —                  | —     | 1                                       | 1      | —       | —       | —       | —       | 1          | 1           | 1                  | 5     | 5  |
| 35-39               | —                                       | —      | 1       | —       | —       | 1       | 1          | —           | —                  | 3     | 1                                       | —      | —       | —       | —       | —       | 1          | —           | 1                  | 3     | 3  |
| 40-44               | 1                                       | —      | —       | —       | —       | 1       | —          | —           | —                  | 2     | —                                       | 1      | —       | —       | —       | —       | 2          | —           | 1                  | 4     | 4  |
| 45-49               | —                                       | 1      | —       | —       | —       | —       | —          | —           | —                  | 1     | —                                       | —      | —       | —       | —       | 1       | 2          | —           | —                  | 3     | 3  |
| 50-54               | 1                                       | 1      | —       | —       | —       | —       | —          | —           | —                  | 2     | —                                       | —      | —       | —       | —       | 1       | 1          | —           | —                  | 2     | 2  |
| 55-59               | —                                       | 2      | —       | —       | —       | —       | —          | —           | —                  | 2     | 1                                       | 2      | —       | —       | —       | —       | 1          | —           | —                  | 4     | 4  |
| 60-64               | —                                       | —      | —       | 1       | —       | 1       | —          | —           | —                  | 2     | 7                                       | 2      | 1       | —       | —       | 1       | 1          | —           | —                  | 12    | 12 |
| 65-69               | —                                       | 1      | —       | —       | —       | —       | —          | —           | —                  | 1     | 2                                       | —      | —       | —       | 1       | —       | —          | —           | —                  | 3     | 3  |
| 70-74               | 1                                       | 1      | 1       | —       | —       | —       | —          | —           | —                  | 3     | 2                                       | 2      | —       | —       | —       | 2       | —          | —           | —                  | 6     | 6  |
| 75-79               | 3                                       | —      | —       | —       | —       | —       | —          | —           | —                  | 3     | 2                                       | —      | —       | —       | —       | —       | —          | —           | —                  | 2     | 2  |
| 80-84               | —                                       | —      | —       | —       | —       | —       | —          | —           | —                  | —     | 2                                       | 2      | —       | —       | —       | —       | —          | —           | —                  | 4     | 4  |
| Total               | 6                                       | 6      | 2       | 1       | —       | 3       | 1          | —           | —                  | 19    | 19                                      | 10     | 1       | —       | 1       | 5       | 9          | 1           | 6                  | 52    | 52 |

Table 14 shows that for the total material more than fifty per cent of the deaths from gall stone disease occurred within a year of the beginning of the disease, and that  $3/4$  of the deaths occurred within 5 years of the onset of the disease. The remaining deaths occurred between 5 and 36 years after the first attack. For the younger patients, the time interval between the onset of the disease and the death is longer than for the older patients. Of those under the age of 50, 11 out of 25 died within 5 years of the beginning of the disease. Of those over the age of 50, 43 out of 46 died within 5 years. The difference is statistically significant (diff. =  $49,5 \pm 10,6\%$ ). In the case of patients who were taken ill in early years, we may therefore assume that the death-risk corresponds more closely with the figures given in the right part of table 13, and that, for the patients who were taken ill in more advanced years, the figures given in the left part of that table illustrate best the actual state of things.

In the foregoing pages we have considered the material in its entirety and only tried to give an idea of the risk of developing gall

stone, the risk of being taken ill, and the risk of dying. We might carry the analysis further and examine the death-risk for a person being taken ill with one form or another of gall stone disease. We might further analyse the risk of falling ill for a person having gall stone, with regard to the risk of falling ill with one form or another of gall stone disease. We might also analyse the risk of relapsing for a person suffering from gall stone disease, in one form or another, and after conservative or operative treatment. This leads us from questions of general population-statistical interest to risk problems which are of practical interest, particularly to the surgeon, and which might therefore be classified as clinical problems. In the following chapter the clinical material is treated with regard to the risk of dying in the different forms of the disease and after different methods of treatment, and further, with regard to the risk of relapsing. Finally, in chapter 7 we shall discuss the risk for a person with gall stone of being taken ill with one form or another of the disease, of getting relapse, and of dying from the disease.

### Summary.

*The risk of developing gall stone, from the point of view of the population,* is present in all age groups. For men, it increases from the ages of 25—34 years to the ages of 35—44 years, then decreases somewhat up to the ages of 55—64 years in order afterwards to increase again. For women, the risk increases up to the ages of 15—24 years, is somewhat smaller in the following age group in order to increase again, attaining its highest value at the ages of 45—54 years. Then the risk decreases somewhat with rising age in order to increase again for the ages over 75.

*The risk of contracting gall stone disease from the point of view of the population* is present during the whole lifetime. It is smaller than the risk of developing gall stone and takes a course fairly parallel to the latter.

*The risk of dying from gall stone disease from the point of view of the population.* The death-risk increases for both men and women with about double the value for each 5-year period from the ages over 35 and onwards. The risk is smaller for men than for women, owing to the fact that men contract gall stone disease to a smaller extent than women.

The *risk of contracting gall stone disease for a person having gall stone*. Between 15 and 50 per cent of those who develop gall stone are taken ill with gall stone disease, men as well as women, at all ages. It is possible that the disease appears after a fairly short interval following the formation of gall stone.

The *death-risk for a person suffering from gall stone disease*. For those falling ill up to the age of 40 years, men as well as women, the risk of dying is about 3 per cent, for those taken ill between 40 and 50, it is doubled (6 per cent), whereupon it increases with rising age. Of those who were taken ill with gall stone disease under the age of 50 and who died from the disease, less than fifty per cent died within 5 years of the beginning of the disease. Of those who were taken ill over the age of 50 and who died from the disease, the majority died within 5 years of the beginning of the disease.



## CHAPTER 5.

### Cases Not Operated On.

#### Indications for conservative treatment.

During the time covered by the investigation, operation was as a rule not advised in the cases in which the patient was being treated for his first attack of gall stone disease, unless a widespread peritonitis, an impending perforation, and so on, forced to operation on vital indications.

To the patients whose anamnesis showed repeated attacks, operation was recommended unless general contraindications against operation were present, for instance diseases of the heart or lungs, advanced age, and reduced general state of health.

In some cases in which the patient was admitted to the hospital in such a desperate condition that, to judge by human standards, an interference could not possibly save him, it was deemed advisable not to operate.

We shall try to analyse below these principles of conservative treatment.

#### The material.

During the years 1922—1935 were treated in the hospital 498 cases of gall stone disease in which the patient was not operated on during the first stay in hospital. The material was divided into two main groups, one comprising so-called non-complicated attacks of biliary colic, termed cholelithiasis below, the other cases of acute cholecystitis (see p. 85). The distribution of the material by age and sex appears in table 15, in which those who died during the stay in hospital are also entered.

The grounds for not operating upon these 498 patients are given in table 16 in so far as they are stated in the diary material. In many cases operation was rejected on several grounds. Under the heading »first attack», for instance, are included a number of cases

Table 15. The clinical material of persons suffering from gall stone disease. Age and deaths at first stay in hospital.

| Age<br>at first<br>stay | Not operated   |        |             |        |        |               |        |             |        |        | Operated    |        |             |        |        |                |        |             |        |        | Not op. + op.          |        |             |        |        |             |        |             |        |        |             |        |             |        |             |        |             |        |
|-------------------------|----------------|--------|-------------|--------|--------|---------------|--------|-------------|--------|--------|-------------|--------|-------------|--------|--------|----------------|--------|-------------|--------|--------|------------------------|--------|-------------|--------|--------|-------------|--------|-------------|--------|--------|-------------|--------|-------------|--------|-------------|--------|-------------|--------|
|                         | Cholelithiasis |        |             |        |        | Cholecystitis |        |             |        |        | All cases   |        |             |        |        | Cholelithiasis |        |             |        |        | Cholecystitis<br>acuta |        |             |        |        | All cases   |        |             |        |        | All cases   |        |             |        |             |        |             |        |
|                         | M              |        | W           |        | Number | M             |        | W           |        | Number | M           |        | W           |        | Number | M              |        | W           |        | Number | M                      |        | W           |        | Number | M           |        | W           |        | Number | M           |        | W           |        |             |        |             |        |
|                         | deaths         |        | deaths      |        |        | deaths        |        | deaths      |        |        | deaths      |        | deaths      |        |        | deaths         |        | deaths      |        |        | deaths                 |        | deaths      |        |        | deaths      |        | deaths      |        |        | deaths      |        | deaths      |        | deaths      |        | deaths      |        |
|                         | among these    | Number | among these | Number |        | among these   | Number | among these | Number |        | among these | Number | among these | Number |        | among these    | Number | among these | Number |        | among these            | Number | among these | Number |        | among these | Number | among these | Number |        | among these | Number | among these | Number | among these | Number | among these | Number |
| 10-14                   | —              | —      | —           | —      | —      | —             | —      | —           | —      | —      | —           | —      | —           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | 1           | —      |             |        |             |        |
| 15-19                   | —              | —      | —           | —      | —      | —             | —      | —           | —      | —      | —           | —      | —           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 4      | —           |        |             |        |
| 20-24                   | 2              | 10     | —           | —      | 1      | 1             | —      | —           | —      | —      | —           | —      | —           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 27     | 1           |        |             |        |
| 25-29                   | 5              | 17     | —           | —      | —      | 2             | —      | —           | —      | —      | —           | —      | —           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 69     | —           |        |             |        |
| 30-34                   | 4              | 8      | —           | —      | —      | 10            | —      | —           | —      | —      | —           | —      | —           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 60     | 1           |        |             |        |
| 35-39                   | 4              | 14     | —           | —      | —      | 7             | —      | —           | —      | —      | —           | —      | —           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 11     | —           |        |             |        |
| 40-44                   | 2              | 11     | —           | —      | —      | 4             | 11     | 1           | 8      | —      | 25          | 1      | —           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 14     | 1           |        |             |        |
| 45-49                   | 2              | 21     | —           | —      | —      | 5             | 10     | —           | 7      | 21     | 2           | —      | —           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 7      | —           |        |             |        |
| 50-54                   | 5              | 14     | —           | —      | —      | 7             | 18     | —           | 9      | 39     | 1           | —      | —           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 12     | 3           |        |             |        |
| 55-59                   | 4              | 15     | —           | —      | —      | 9             | 19     | —           | 14     | 33     | —           | —      | —           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 5      | 1           |        |             |        |
| 60-64                   | 2              | 12     | —           | —      | —      | 9             | 34     | 1           | 13     | 1      | 49          | 1      | 3           | —      | 9      | 1              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 14     | 1           |        |             |        |
| 65-69                   | 9              | 11     | —           | —      | —      | 10            | 30     | 1           | 12     | 42     | 1           | —      | —           | —      | 4      | 5              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 7      | —           |        |             |        |
| 70-74                   | 5              | 5      | —           | —      | —      | 20            | 1      | 35          | 4      | 29     | 1           | 46     | 4           | —      | 5      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | 13     | 5           |        |             |        |
| 75-79                   | —              | 2      | —           | —      | —      | 9             | 1      | 26          | 3      | 14     | 1           | 31     | 3           | —      | 1      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | —      | 2           | 2      |             |        |
| 80-84                   | 1              | 3      | —           | —      | —      | 7             | 2      | 8           | 1      | 7      | 2           | 10     | 1           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | —      | 3           | 3      |             |        |
| 85-89                   | —              | —      | —           | —      | —      | 3             | —      | 8           | 4      | 4      | —           | 11     | 4           | —      | —      | —              | —      | —           | —      | —      | —                      | —      | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | —      | 4           | —      |             |        |
| Total                   | 45             | 144    | —           | —      | —      | 88            | 5221   | 15133       | 5365   | 1513   | 148         | 113    | 164         | 335    | 8202   | 1817           | 371    | 978         | 12485  | 31211  | 17850                  | 46     | —           | —      | —      | —           | —      | —           | —      | —      | —           | —      | —           | —      | —           | 1      | —           |        |

in which advanced age was a contributory cause of the operation being avoided. Similarly, many of the patients now brought together under the heading »cause not stated», should most likely belong to some one of the other groups, particularly to the group comprising those who refused to let themselves be operated upon. Table 15 shows that a very large part of the material belongs to the more advanced age groups, which is also seen in the fact that the average age of the cases not operated on is 54,4 years (about 7 years higher than that of the cases operated on, 47,0 years).

Table 16. *Grounds for not operating on the patient.*

|                                               |              |
|-----------------------------------------------|--------------|
| First attack, or mild attacks .....           | in 220 cases |
| Disease of the heart .....                    | „ 12 „       |
| Other disease .....                           | „ 34 „       |
| Obesity .....                                 | „ 29 „       |
| Advanced age, reduced general condition ..... | „ 50 „       |
| Refuses operation .....                       | „ 68 „       |
| Cause not stated .....                        | „ 85 „       |
|                                               | Total 498 „  |

### Hospital treatment.

Of the 498 cases, 189 belong to the group of cholelithiasis; out of these, none died during the stay in hospital. Of the 309 cases belonging to the group of acute cholecystitis, on the other hand, 20 died during the stay in hospital. Of these 20 cases, 19 were over 55 years old; more than half of those who died (11 in number) were over 70, and 7 were over 75 years old.

A close analysis of the past histories of the patients who died, made in order to find out whether one or several of the deaths might reasonably be considered as due to the conservative therapy being carried too far, shows as follows:

#### I. Five patients died during the first 24 hours of their stay in hospital.

1) B 623/1923. Woman, aged 84. Repeated attacks of pain for 6 weeks, latest attack the night before day of admittance.

Strongly affected. Temperature 39° C. Tenderness and rigidity over the region of the gall bladder. Died 11 hours after admittance.

Autopsy: gangrenous cholecystitis, perforation of the gall bladder, and diffuse peritonitis.

2) 1642/1928. Woman, aged 65. Gall stone attacks for several years, latest attack one week prior to admittance.

Affected. Mild jaundice. Temperature  $38.8^{\circ}\text{C}$ . Tenderness and rigidity over a resistance, the size of an orange, in the region of the gall bladder. In the course of the day a rapid change for the worse and death.

Autopsy: an abundance of stones in the gall bladder and common bile duct; a number of cholangitic abscesses in the liver; fatty necroses in the pancreas.

3) 113/1932. Man, aged 79. First attack, which began 9 days prior to admittance.

Weak. Severe jaundice. Temperature  $39^{\circ}\text{C}$ . Peritonitis in the upper right part of the abdomen. Died within 24 hours.

Autopsy: acute cholecystitis, diffuse, purulent peritonitis, stone in the common bile duct; myocarditis and cardio-arteriosclerosis.

4) 1191/1932. Man, aged 73. Attacks of biliary colic for 3 weeks.

Affected. Mild jaundice. Temperature  $39^{\circ}\text{C}$ . Circumscribed peritonitis in the upper right part of the abdomen. Died within 24 hours.

Autopsy: Acute cholecystitis, cholangitis, stone in the common bile duct, circumscribed fibrinous peritonitis.

5) 1031/1933. Woman, aged 84. Attacks of gall stone colic for half a year; latest attack began 5 days prior to admittance.

Weak, cyanotic and dyspneic. Jaundice. Temperature  $39^{\circ}\text{C}$ . Diffuse peritonitis, most marked over the region of the gall bladder.

Autopsy: gangrenous cholecystitis with perforation of the gall bladder, diffuse, purulent peritonitis, stone in the common bile duct; bronchopneumonias.

In none of these cases could an operation have saved the patient with any degree of probability.

## II. Four patients died within 48 hours of their stay in hospital.

6) A 427/1924. Woman, aged 64. First attack, setting in 2 days prior to admittance.

Considerably affected, fat and cyanotic. Temperature  $38.8^{\circ}\text{C}$ . Circumscribed peritonitis in the upper right part of the abdomen.

Autopsy: gangrenous cholecystitis, myocarditis, and arteriosclerosis.

7) B 631/1924. Man, aged 65. Isolated attacks of biliary colic for 34 years, latest attack 6 days prior to admittance.

General state of health satisfactory, fat. Temperature  $37.6^{\circ}\text{C}$ . Tenderness over the region of the gall bladder. In the evening of the day of admittance a shaking chill, attended by coma and anuria.

Autopsy: empyema in the fibrin-covered gall bladder; fatty heart.

The rapid deterioration followed by coma and anuria seems to indicate the presence of an acute hepatic insufficiency, in all probability inaccessible to therapy, at least with the scientific resources available at that date.



8) 1702/1929. Man, aged 57. Had had an attack accompanied by jaundice 3 months previously, a new attack 14 days before admittance to hospital.

Slightly affected. Moderate jaundice. Temperature  $39^{\circ}\text{C}$ . The day after admittance a shaking chill, collapse, and after 12 hours, death.

»The patient's condition at admittance was such that operation was immediately considered to be indicated. After a change for the worse the following day, the condition was too poor to allow of operation.»<sup>1)</sup>

Autopsy: chronic cholecystitis, widespread purulent cholangitis; cardio-arteriosclerosis.

9) 1395/1930. Woman, aged 70. First attack of biliary colic, setting in while the patient was being treated in the hospital for a fracture of the neck of the femur. The abdominal symptoms rapidly increased. The temperature rose to  $39.7^{\circ}\text{C}$ . »No operation possible owing to extremely poor general condition.»<sup>1)</sup>

Autopsy: acute gangrenous cholecystitis; gastric ulcer with heavy bleeding. The immediate cause of death was the gastric hemorrhage.

An operation naturally would have had no effect in any of the cases of this group.

III. This group of cases comprises such as lived longer than 48 hours after being admitted to hospital, but in which operation was from the first considered to be of no avail on account of the patient's poor general condition.

10) 325/1925. Woman, aged 74. First attack, setting in 3 weeks previously.

Affected, cachectic. Temperature  $38.2^{\circ}\text{C}$ . Peritonitis in the right part of the abdomen, most marked in the region of the gall bladder. — The day after admittance rapid change for the worse, shaking chills. »Too poor to operate on.»<sup>1)</sup> — Died 48 hours later.

Autopsy: gangrenous cholecystitis with circumscribed peritonitis and sub-phrenic abscess; myocarditis; cardio-arteriosclerosis; purulent bronchitis.

11) 2636/1927. Woman, aged 82. Suddenly taken ill. Considerably affected, confused, slightly jaundiced. Temperature  $38.4^{\circ}\text{C}$ . Extensive resistance at the site of the gall bladder. — »The patient's extremely poor condition does not allow of any real examination — unconscious practically the whole time.»<sup>1)</sup> Died after 7 days.

Autopsy: gangrenous cholecystitis, purulent cholangitis, liver abscesses, circumscribed purulent peritonitis; cardio-arteriosclerosis.

12) 2271/1930. Man, aged 75. While convalescing from prostatectomy he had an attack of acute cholecystitis: within 24 hours coma and anuria. Died 3 days after being taken ill.

Autopsy: gangrenous cholecystitis; adhesive pericarditis; nephrosclerosis.

13) 1719/1933. Woman, aged 67. First attack, setting in 3 days prior to admittance.

<sup>1)</sup> Quoted from the hospital diary.

Affected, jaundiced, fat. Temperature 38° C. Abdomen distended, not tender. The day after admittance comatose. Died after 7 days in an increasingly cholemic condition.

Autopsy: chronic cholecystitis, stone in the common bile duct, liver abscesses; double-sided pyelonephritis; myocarditis; bronchial ectasies with purulent bronchitis.

14) 3578/1934. Woman, aged 81. First attack, setting in 4 days prior to admittance.

Extremely poor condition. Temperature 39° C. Peritonitis in the right upper part of the abdomen. »No thought of operation on account of age and debility.«<sup>1)</sup> Died after 9 days.

Autopsy: gangrenous cholecystitis with perforation to the transverse colon; subphrenic abscess; myocarditis; cardio-arteriosclerosis.

The comparatively prolonged course in this case suggests that a cholecystostomy was indicated, although the possibility of saving the patient no doubt must be considered as extremely small.

Of the cases included in this group, operation seems to have been indicated in the last case only.

IV. This group comprises the cases in which an expectant treatment was thought to be indicated. The symptoms subsided at first, but the patient died, either because of an unexpected acute change for the worse, or owing to complications from other organs.

15) 1239/1931. Woman, aged 76. 3 attacks of biliary colic in 5 years, latest attack 3 days previously.

Affected, jaundiced. Temperature 38.6° C. Marked tenderness over the gall bladder. — Condition unchanged for 3 days; died the 4th day from bronchopneumonia.

Autopsy: gangrenous cholecystitis; bronchopneumonia, myocarditis.

16) 1941/1931. Woman, aged 65. Attacks of biliary colic for 7 years, latest attack 2 days prior to admittance.

Strongly affected, slightly jaundiced. Temperature 39.7° C. Tenderness and rigidity in the right upper quadrant of the abdomen. The symptoms subsided during the next few days. — One week following admittance the patient died from sudden weakness of the heart. No autopsy was performed.

17) 1279/1932. Woman, aged 66. First attack, setting in 2 days prior to admittance.

Affected, cyanotic. Temperature 38.5° C. Tenderness and slight rigidity over the region of the gall bladder. — The symptoms of peritonitis gradually

<sup>1)</sup> Quoted from the hospital diary.

decreased the first days. On the 6th day after admittance the temperature began to rise; the abdomen was soft and slightly tender. Died the following day. — »Insufficient ground for operating on the fat and cyanotic patient during the first days, when the temperature was moderate and not increasing, and the symptoms of peritonitis decreased more and more. When the temperature began to rise the day before death occurred, the symptoms of peritonitis had disappeared, the abdomen was soft, and the tenderness only slight but the cyanosis had increased. Still there was no reason to operate, the less so as the general state of health and the heart were contraindicated.»<sup>1)</sup>

Autopsy: acute cholecystitis without peritonitis; cardio-arteriosclerosis, myocarditis.

18) 2337/1934. Woman, aged 58. Attacks of biliary colic for 3/4 year, latest attack one week prior to admittance.

General condition strongly affected, mild jaundice. Temperature 40.8° C. Tenderness and rigidity over the region of the gall bladder. Diastase value in the urine: at least 2048. — The symptoms subsided the next few days; on the 6th day sudden death.

Autopsy: ulcerous cholecystitis, stone in the common bile duct, hemorrhagic pancreatitis; coronary thrombosis, myocarditis and cardio-arteriosclerosis.

19) 2165/1935. Woman, aged 73. First attack of biliary colic, setting in 2 days prior to admittance.

General condition satisfactory, fat. Temperature 37.9° C. Tenderness over the region of the gall bladder. Diastase value in the urine: 2048. — The temperature became normal in three days, whereupon the patient was discharged for treatment in another hospital. — 6 weeks later a new attack; simultaneously cardiac insufficiency. Was again admitted to the hospital the day after the attack had set in. Cyanotic and dyspneic; edema in the legs. Moderate tenderness and slight rigidity over the region of the gall bladder. Subfebrile. After 11 days the temperature, which had previously been subfebrile, suddenly rose to 39.4° C; increased dyspnea; died 24 hours later.

Autopsy: acute cholecystitis; fatty heart.

In this case the picture of the disease was dominated by the cardiac insufficiency which contraindicated operation. The changes in the gall bladder found in the post-mortem examination were of fairly moderate nature.

The lethal issue could surely not have been prevented in any of these cases by an operative intervention.

V. Finally the diagnosis was to a certain degree incorrect in one case.

20) 2224/1927. Woman, aged 36. While the patient was treated for heart disease in the medical department of the hospital, she had repeated attacks of biliary colic and was therefore transferred to the surgical department on August 20.

<sup>1)</sup> Quoted from the hospital diary.

Affected, slightly jaundiced. Cyanotic and dyspneic. Temperature 38.7° C. Vitium cordis. Marked tenderness and rigidity in the upper part of the abdomen, most pronounced over the region of the gall bladder. Diastase value in the urine: 256. — Aug. 30. shaking chill, temperature 40.5° C; new attack. Aug. 31. the temperature normal in the evening. The patient was taken to the medical department.

Sep. 2. On account of a new attack with chill and a temperature of 40.4° C, the patient was again admitted to the surgical department. »Too poor to operate on. The abdominal symptoms never alarming.« Death on Sep. 4.

Autopsy: gangrenous cholecystitis, stone in the common bile duct, purulent cholangitis, widespread purulent pancreatitis; hypertrophy of the heart, chronic endocarditis.

In this case the immediate cause of death was the acute pancreatitis. In spite of the grave changes in the gall bladder and the pancreas observed in the post-mortem examination, the abdominal symptoms were so moderate during the patient's first stay in the surgical department that operation was not considered to be indicated. However, when the patient in connection with a new attack on Aug. 30 had a shaking chill and high temperature, an operation ought to have been performed in spite of the patient's cardiac insufficiency.

The account of the deaths shows that among those who died during the stay in hospital (all of whom had acute cholecystitis), operation was possibly indicated only in two cases (Nos. 14 and 20). In one of these cases (No. 20) the situation seems to have been misjudged; in the second case the patient was 81 years old. Although the possibility of saving one of these patients by an operation must be considered to have been small, it is not altogether excluded that an interference might have had the desired effect in one or the other case. The operation to be contemplated naturally would have been the simplest possible, that is to say cholecystostomy.

The indications for conservative treatment given above, p. 70, thus were perhaps somewhat too narrow. A contributory cause of the relatively high mortality of the cases not operated on is that among them were found no less than 7 cases with stone in the common bile duct attended in 5 cases by cholangitis, liver abscess or acute pancreatitis.

Several of the histories of disease given above (e. g. Nos. 8, 13 and 20) show that the clinical symptoms of acute cholecystitis in



some cases were considerably less grave than the corresponding autopsy finding. (The same may be observed in operations of such cases.) In our material it was chiefly in elderly patients that this discrepancy between the clinical finding and the morbid process was present. Similar experiences have been made by other writers (e. g. ANDREWS, MENTZER, TOUROFF, JUDD & PHILLIPS.) This fact might also to a certain extent speak in favour of widening the indications for operation, as there is a risk of regarding the morbid process as more innocent than it actually is.

In old and often weak patients, however, the postoperative mortality is fairly high, even if cholecystostomy only is performed. Consequently it is not excluded that widened indications for operation would result in an increased mortality, as some patients who might have recovered by conservative treatment, would die after an operation. As, further, the cases in the material in which the conservative therapy was maybe carried too far, are very few in number (2 during a time of 14 years), the author cannot but reach the conclusion that *the stated contraindications against operation were best suited to the material.*

### Re-examination.

As compared to the very numerous investigations published on the subsequent histories of patients operated on for gall stone disease, available re-examinations of cases not operated on are very few. The majority of such examinations originate from *internal* departments, as is quite natural. In an re-examination of 96 cases, BINDER (1902) found that 11 had died from gall stone disease. In a statistical survey of 1903, quoted by RIEDEL, the deaths from gall stone diseases amount to 125 out of 1000 cases. In 1924, TALLQVIST published the results of an examination of 206 cases. Data were obtainable on 110 cases (the average time of observation was 6 years), and among these, 9 had died from gall stone disease and 24 had been operated on for this disease; 4 of the deaths were post-operative. JAGUTTIS (1926) re-examined 114 out of 260 cases, with a time of observation of at least 10 years. Of these 114 cases, 13 had died from gall stone disease not operated on and 26 had been operated on (4 deaths). Of 58 patients not operated on, and alive at the time of re-examination, 43 (74 per cent) were free

from symptoms, whereas the remaining 15 cases suffered from more or less severe discomforts. In papers published in 1927 and 1928, LOEWENBERG, NOAH, and SCHERK presented the results of an individual re-examination of 208 out of 527 cases. Half of these 208 cases had been observed during a shorter time than 2 years, the remaining cases between 2 and 7 years. 19 of the cases had been operated on, 5 suffered from other diseases as well, and of the remaining 184, 34 (18 per cent) were altogether free from symptoms, 37 (20 per cent) had only mild discomforts, 74 (40 per cent) had moderately severe, and 39 (21 per cent) severe, discomforts. BLACKFORD, KING and SHERWOOD, who in 1933 re-examined 200 cases (60 per cent of the material) of «chronic cholecystitis» with a time of observation of 5—15 years, found satisfactory results in 37 per cent of the cases, and severe discomforts in 49 per cent (part of these cases had been operated on), while 15 per cent of the cases had died, but only 1 per cent from gall stone disease.

Only a few re-examinations of conservatively treated cases originate from *surgical* departments. In 1921, NORDMANN re-examined 52 cases of acute cholecystitis and found only 3 which were free from symptoms; 17 cases had been operated on later, 20 still suffered from attacks, and 12 from permanent discomforts. BARDY (1924), who re-examined 75 of 118 cases, found 17 (22,7 per cent) to be free from symptoms, whereas 49 (65 per cent) had attacks, 3 had died from the disease, and 5 had been operated on. LIEBERG (1937) re-examined 244 cases of acute cholecystitis, treated in the surgical clinic in Lund and not operated on. Half of the material had been under observation between 2 and 5 years, the remaining cases between 5 and 12 years. Of all the cases, 94 (38,5 per cent) were free from symptoms, 61 (25,0 per cent) had mild discomforts, whereas 89 (36,5 per cent) either had severe discomforts, had been operated on for, or died from, the gall stone disease.

To get a clearer survey the abovementioned examinations are brought together in table 17.<sup>1)</sup> It goes without saying that no definite conclusions can be drawn from BINDER's and RIEDEL's brief communications. Of the other re-examinations, those carried out by

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<sup>1)</sup> The percentage figures given in the table in some cases differ from the ones quoted above according to the different authors as in the table they have been recalculated in relation to the total re-examined material.

Table 17. *Re-examination of cases not operated on. Data from the literature.*

| A u t h o r                                       | Number of cases<br>N | Re-examined of these<br>n | Time of observation                            | Free from symptoms |        | Mild symptoms |        | Severe symptoms |        | Operated on |        | Deaths from gall stone disease |        | Deaths from other disease <sup>1</sup> |        |
|---------------------------------------------------|----------------------|---------------------------|------------------------------------------------|--------------------|--------|---------------|--------|-----------------|--------|-------------|--------|--------------------------------|--------|----------------------------------------|--------|
|                                                   |                      |                           |                                                | Numb.              | % of n | Numb.         | % of n | Numb.           | % of n | Numb.       | % of n | Numb.                          | % of n | Numb.                                  | % of n |
| BINDER (1902).....                                | —                    | 96                        | —                                              | —                  | —      | —             | —      | —               | —      | 7           | —      | 11                             | —      | —                                      | —      |
| Quot. by RIEDEL (1903)                            | —                    | 1000                      | —                                              | —                  | —      | —             | —      | —               | —      | —           | —      | 125                            | 12,5   | —                                      | —      |
| TALLQVIST (1924) .....                            | 206                  | 110                       | on an average 6 years                          | —                  | —      | —             | —      | —               | —      | 24          | 21,8   | 9                              | —      | —                                      | —      |
| JAGUTIS (1926) .....                              | 260                  | 114                       | at least 10 "                                  | 43                 | 37,7   | —             | —      | 15              | 13,2   | 26          | 22,8   | 13                             | —      | —                                      | —      |
| LOEWENBERG, NOAH & SCHERCK (1927) .....           | 527                  | 208                       | under 2 " <sup>4)</sup><br>2-7 " <sup>4)</sup> | 34                 | 16,3   | 111           | 53,4   | 39              | 18,8   | 19          | 9,1    | —                              | —      | —                                      | —      |
| BLACKFORD, KING & SHERWOOD <sup>1</sup> (1933)... | >300                 | 200                       | 5 15 "                                         | 73                 | 36,5   | —             | —      | 54              | 27,0   | 43          | 21,5   | 2                              | 1,0    | 28                                     | 14,0   |
| NORDMANN <sup>2</sup> (1921).....                 | —                    | 52                        | —                                              | 3                  | 5,8    | —             | —      | 32              | 61,5   | 17          | 32,7   | —                              | —      | —                                      | —      |
| BARDY (1924) .....                                | 118                  | 75                        | —                                              | 17                 | 22,7   | —             | —      | 49              | 65,3   | 5           | 6,7    | 3                              | 4,0    | —                                      | —      |
| LIEDBERG <sup>3</sup> (1937) .....                | 251                  | {127<br>117               | 2-5 years<br>> 5 "                             | 64                 | 50,4   | 27            | 21,3   | 23              | 18,1   | 8           | 6,3    | 5                              | 3,9    | (34) <sup>3)</sup>                     | —      |
|                                                   |                      |                           |                                                | 30                 | 25,6   | 34            | 29,1   | 19              | 16,2   | 25          | 21,4   | 9                              | 7,7    |                                        |        |

<sup>1)</sup> Only non-complicated cases.

<sup>2)</sup> Only cases of acute cholecystitis.

<sup>3)</sup> Entered under the headings: free from symptoms — mild symptoms — severe symptoms.

<sup>4)</sup> Half the material.

From internal departments  
From surgical departments

TALLQVIST, JAGUTTIS, and LOEWENBERG, NOAH and SCHERK refer to a total material of cases of gall stone disease treated in internal departments. It is, however, difficult to estimate the value of the data given, as only a small part of the available material, as a rule hardly half of it, was subjected to re-examination. It seems improbable that the given data on persons who later died from the disease or were operated on, actually represent only the part of the material which was selected at random for re-examination: as a rule it is considerably easier to obtain information on patients who have been subjected to a new operation or who have died. Under such circumstances we cannot simply exclude the possibility that deaths and cases operated on were to a larger extent included in the material of re-examination than patients who subsequently were free from symptoms or had mild discomforts. Consequently there are reasons to suspect that an re-examination based on data referring to only a comparatively small part of the material will give essentially too high figures for cases subsequently operated on and for deaths. Be that as it may, only a limited value can be ascribed to re-examinations which give information on such a small part of the treated patients as the ones quoted above.

BLACKFORD, KING and SHERWOOD re-examined cases of »chronic cholecystitis», that is to say such cases as are here termed cases of non-complicated cholelithiasis. This re-examination only covers 60 per cent of the material; consequently, its value should be considered as limited.

Among writers who have re-examined materials from surgical departments, NORDMANN does not give information on the percentage of his total material that was re-examined; BARDY gives data on 63 per cent of the material only.

In 1931 the present author published a preliminary report in which I tried to show that the prognosis was considerably more favourable for patients suffering from gall stone disease who had had only one attack, than for those who had had several attacks. The material covered 94 cases, treated in the surgical clinic in Uppsala during the periods Sep. 1, 1916—Aug. 31, 1918, and Sep. 1, 1921—Dec. 31, 1929. The author has subsequently continued these examinations and has been able to obtain more reliable data and a more comprehensive material (when planning the investigation, the author from the first aimed at collecting a representative material). An



examination of the problem of the relapses among cases not operated on seemed the more justified as the investigations then available on cases not operated on were very defective; consequently, definite criteria for making prognoses in cases not operated on were actually lacking.

Later an investigation into cases treated for acute cholecystitis was published by LIEBERG in 1937. LIEBERG's material differs favourably from those published by earlier investigators in that it includes the best part of the primary cases (97.2 per cent). It might be objected to this investigation that the time of observation was short. For half of the material, it only covered 2—5 years, and as we intend to show below, only that part of the material was subjected to a sufficiently long observation which includes the cases that were re-examined at least 5 years after the first stay in hospital. LIEBERG adopted the same principles of division as those followed in the abovementioned paper published by the author in 1931: he distinguished between patients who were treated for their first attack of gall stone disease, and patients who had had repeated attacks. As LIEBERG's investigation undoubtedly is the most important of the ones so far available, we shall return to it below.

In summing up we may state that the investigations here reviewed which refer to a total material of patients not operated on, have two shortcomings. Only a comparatively small part of the treated patients were re-examined. We have pointed out above that figures for the tendency to relapse, etc., obtained from such materials, have only a limited value. Further, the materials have not been grouped according to the various forms of gall stone disease that have occurred. As the cases from a prognostic point of view may vary in character, total figures which have not been subjected to a close analysis, are obviously of little value.

A detailed analysis of a sufficiently large material of cases not operated on, however, ought to give important data on the tendency to relapse in different forms of the disease and in different stages; in our opinion, such an analysis therefore would be of definite value.

#### *The author's material.*

Of the cases not operated on in the Uppsala material, the author has re-examined those who were treated in the years 1922—1930.

The total number of cases not operated on during the first stay in hospital in this period amounted to 226. Of these, 10 died during the stay in hospital (they are included in the account of the primary deaths given above). To the remaining 216 patients a questionnaire was sent to the following effect:

Have you had any more attacks of biliary colic or similar attacks, and in that case when? Nature of attacks: Mild or severe pains? In what part of the abdomen did you feel the pains? How long have the attacks lasted? Have they been attended by: Fever? Chills? Vomitings? Constipation? Jaundice? Urination discomforts? Blood in the urine? Dark urine? Have you felt tenderness in the abdomen on finger pressure in connection with the attacks, and where? How long did you have to stay in bed because of the attacks? How were they treated?

Have you had prolonged (chronic) discomforts from the stomach without connection with definite attacks? Pains in the abdomen? Constant? Temporary? Dull, like toothache? Sharp? Radiating, where? In what part of the abdomen are the pains felt? Middle? Pit of the stomach? Right upper, right lower, portion? Left upper, left lower, portion? Do the pains move from one place to another? How? Do the pains set in in connection with: Meals? Evacuation of the bowels? Any particular position of the body, what position? Bodily exercise? Exertion? Have you had jaundice in connection with the pains? Do you feel tenderness in the abdomen on finger pressure, and where? Do you feel tender in the small of the back (to the left, right, on both sides of the spinal column)? Have you suffered from: Eructations? Gas? Nausea? Vomitings? Are these discomforts related to meals? How? Have you had constipation or diarrhea?

What is your present state of health? Do you feel quite well? Have you put on or lost flesh? How is your sleep? What kind of work do you perform? Feces: how often? Character (hard, ordinary, loose)? Does mucus appear in the feces? Do you use aperients; in that case what kind, and how often? Urine: How often? Pains, burning, or discomforts at urination? Dark-coloured urine? Have you been treated by a physician for your disease, and in that case by whom (in what hospital), and when? Have you been operated on for your disease (when and where)?

The re-examination was carried out partly in the year 1931, partly in 1935 and 1936; in 1937 certain supplementary examinations were made. Data were obtained on 209 of the 216 patients (96,8 per cent). The 7 patients about whom no information could be obtained, were all of them unknown to the register offices in question; they were altogether left out in the treatment of the material. It is not probable that these cases, excluded at random, have been capable of affecting the result of the re-examination.

In estimating the patient's condition after the stay in hospital we chiefly must pay attention to the presence, or absence, of attacks of pain, irrespectively of the attacks being of very short duration or more prolonged. The data on such attacks given by the patients should be considered as comparatively reliable, and the time can often be fixed fairly exactly. The more chronic discomforts, often dyspeptic in character, which not infrequently occur in persons suffering from gall stone disease, are often difficult definitely to relate to the disease. In the cases where it seems probable that they were caused by gall stone disease, regard to these symptoms is naturally paid.

For the sake of brevity, we use in the following the term *relapse* to denote that the patient again had symptoms of his disease, either in the form of attacks of pain or of more chronic discomforts.

The data on the risk of relapse in a disease, which are obtainable by an re-examination, are dependent on whether the time of observation is sufficiently long. In table 18 the cases are grouped according to the length of the time of observation and also according to the time which elapsed between the first stay in hospital and the first relapse. In a number of cases it is only stated that new attacks had been present, but no data are given as to the date at which they occurred. These cases were entered separately under the heading »new attacks». Also, there are no certain data on the time at which possible relapses occurred in the case of patients who died after the stay in hospital. These cases were therefore brought into a separate group.

The table shows that more than half of the first relapses occurred within the first year of the stay in hospital, but that relapses may occur even up to nine years afterwards. Only 75,6 per cent of the relapses occurred within 3 years, 81,7 per cent within 4 years, 90,2 per cent within 5 years, and 96,3 per cent within 6 years.

*If an re-examination is to afford a reliable survey, the time of observation thus ought to be at least 5 years and if possible somewhat longer, as at least 10 per cent of the relapses do not occur until 5 years have elapsed. — In our own material, the average time of observation is 6,9 years; as only a few cases (14) were observed during a shorter time than 5 years, the data on the frequency of relapse to be obtained from this material will no doubt correspond fairly closely to the actual frequency.*

Table 18. *Time of relapse after first stay in hospital. Cases not operated on.*

| Groups                                        | Re-examination after number of years |    |    |    |    |   |    |             |     | Total |
|-----------------------------------------------|--------------------------------------|----|----|----|----|---|----|-------------|-----|-------|
|                                               | 4                                    | 5  | 6  | 7  | 8  | 9 | 10 | 11 and over |     |       |
| Attack within ½ year .....                    | 5                                    | 7  | 7  | 11 | 2  | 1 | —  | 2           | 35  |       |
| » » 1 » .....                                 | —                                    | 4  | 5  | 2  | 3  | — | —  | —           | 14  |       |
| » » 2 years ...                               | —                                    | 2  | 1  | —  | 2  | — | —  | 1           | 6   |       |
| » » 3 » .....                                 | 2                                    | —  | 3  | 1  | —  | — | 1  | —           | 7   |       |
| » » 4 » ...                                   | —                                    | 1  | 2  | 1  | —  | — | 1  | —           | 5   |       |
| » » 5 » ...                                   | —                                    | 1  | 1  | 2  | —  | — | —  | 3           | 7   |       |
| » » 6 » ...                                   | —                                    | —  | 1  | 4  | —  | — | —  | —           | 5   |       |
| » » 7 » ...                                   | —                                    | —  | —  | 1  | —  | — | 1  | —           | 2   |       |
| » » 8 » ...                                   | —                                    | —  | —  | —  | —  | — | —  | —           | —   |       |
| » » 9 » ...                                   | —                                    | —  | —  | —  | —  | — | 1  | —           | 1   |       |
| » » 10 » ...                                  | —                                    | —  | —  | —  | —  | — | —  | —           | —   |       |
| » » 11 » ...                                  | —                                    | —  | —  | —  | —  | — | —  | —           | —   |       |
| new attacks .....                             | 1                                    | 7  | 5  | 8  | 3  | 4 | —  | 5           | 33  |       |
| healthy .....                                 | 6                                    | 7  | 23 | 12 | 11 | 3 | 2  | 2           | 66  |       |
| deaths after discharge<br>from hospital ..... | —                                    | 20 | 4  | 1  | —  | 1 | 1  | 1           | 28  |       |
| Total                                         | 14                                   | 49 | 52 | 43 | 21 | 9 | 7  | 14          | 209 |       |

The material is divided into two main groups:

1) Cases of *clinically non-complicated cholelithiasis*.

2) Cases of *acute cholecystitis*. In the latter cases, the temperature was at least  $38^{\circ}\text{C}$ ; the clinical symptoms were tenderness and rigidity over the region of the gall bladder, and in the majority of the cases also resistance in this region. In this group are included 18 cases which were complicated by acute pancreatitis. The latter was diagnosed by an X-ray examination or a pathological diastase value in the urine. The pancreatitis appeared in the clinical picture only as a complication to the cholecystitis. A treatment of these 18 cases as a separate group proved not to give any unequivocal results and they are therefore brought together with the cases of cholecystitis.

In this group, as possibly also in the preceding group, some cases are further found which had stone in the common bile duct. Of the cases subjected to a post-mortem examination (19 in number), common duct stone was present in 7.



Probably, stone in the common bile duct was not present with equal frequency among the other cases not operated on. We have reason to suppose that the frequency of stone in the common bile duct among patients not operated on is of the same order of magnitude as that among patients operated on, that is to say between 15 and 20 per cent (see below, p. 146, where this question is discussed in greater detail).

In each of the abovementioned main groups, the material is divided according to the following principles:

- A. *With regard to the state of health after the discharge from hospital.*
  - I. Those who were clinically healthy. To this group are referred a) the patients who after the discharge from hospital had had neither attacks of pain nor other morbid symptoms which could reasonably originate from the gall stone disease (66 cases), b) those who after the discharge had occasionally had an isolated and mild attack of biliary colic but otherwise were quite healthy and fit for work (32 cases).
  - II. Those who had mild discomforts. These patients had had attacks of biliary colic which as a rule had been infrequent and often mild, not affecting the patient's capacity for work (18 cases),
  - III. Those who had severe discomforts from the disease. These patients had had either repeated attacks of biliary colic or other discomforts from the gall stone disease, causing their health and capacity for work to be impaired or lost (19 cases). In this group are also included the patients who had later been operated on for their disease (46 cases) or who had died from the disease (5 cases).
- B. *With regard to the number of attacks of biliary colic to which the patient had been subjected at the admittance to the hospital.*
  - I. Those who had been treated for their first attack of biliary colic. As a first attack is counted a) an isolated attack, b) a series of attacks during a period of one month at most. It is very frequently stated by the patient that he has had repeated attacks of biliary colic during a short time before the admittance to hospital (as also frequently

happens in the case of attacks of renal colic). It seems inadequate to distinguish between the patients who had been admitted to hospital for their first attack in the strict sense of the term, and those who had had repeated attacks during a short period. A time limitation of one month seems advisable for practical reasons. Of the 92 patients referred to this group in our material, 76 were admitted for attacks of biliary colic which had lasted less than a week, 7 for attacks which had lasted for 2 weeks, 4 for attacks lasting for 3 weeks, and 5 for attacks lasting for one month.

- II. Those who had been treated for their second attack of biliary colic, provided that the attacks had been distinctly separated by a free interval of at least one month. Of the 21 cases belonging to this group, the free interval was 2 months in 3 cases, 3 months in 1 case, 6 months in 1 case, 1 year in 4 cases, 2 years in 5 cases, 3, 4 and 5 years in 1 case each, and finally 7 and 10 years in 2 cases each.
- III. Those who had been treated for their third, fourth, etc., attack. The data available in the diaries do not allow of a detailed grouping of the material according to the principles stated under B. except in the case of patients who were treated for their first or second attack of biliary colic: in a large number of the remaining cases it is only stated that the patient had had repeated attacks during a given time.

*Those who died after the first stay in hospital.*

Before entering on an account of the state of health of the surviving patients, we shall briefly discuss those who died during the time of the re-examination.

28 patients had died after the first stay in hospital; of these 5 from gall stone disease or a disease possibly related to the former. These 5 cases were:

A 533/1924. Woman, aged 72, died 1 year after discharge from cholecystitis and myocarditis.

A 715/1924. Woman, aged 74, died 5 years after discharge from cholecystitis.

2017/1928. Woman, aged 76, died half a year after discharge from cancer of the gall bladder.

3272/1928. Woman, aged 55, died 2 1/2 years after discharge from cancer of the gall bladder.

2733/1930. Man, aged 76, died 2 weeks after discharge from acute pancreatitis and diabetes.

The remaining 23 cases died of other diseases:

disease of the heart: 1 man, 4 women,

disease of the lungs: 7 women,

cerebral hemorrhage: 3 men, 1 woman,

diabetes: 1 woman,

sepsis: 1 woman,

marasmus senilis: 2 women,

cancer of other organs: 3 women.

Of the 28 patients who died after the discharge from hospital only the five who died of gall stone disease or of cancer of the gall bladder were included in the following treatment of the material. The points in favour of a correlation between gall stones and cancer of the gall bladder are not convincing, it is true, but many scientists still think that there exists a connection between the two diseases (COURVOISIER, KAZAMA, LENTZE, GRAHAM, PETROV and KROTKINA, ILLINGSWORTH a. o.) and consequently, so as to be on the safe side we consider that the two patients who died of cancer of the gall bladder ought to be included among those who died from gall stone disease. The other 23 deaths, on the other hand, are not included, and for two reasons: in the first place, we do not have quite reliable data for all of them as to the occurrence of possible attacks between the discharge from hospital and the time of death, secondly the subsequent duration of life for these cases was barely 4 years on an average, a period which according to what was stated above (p. 84), is too short for the risk of relapse to be estimated with a fair degree of probability.

#### *The remaining cases.*

Inclusive of the 5 cases which died of gall stone disease there remain 186 cases, 66 of which belong to the group of cholelithiasis, and 120 to the group of cholecystitis.

Out of the total material, 98 patients (52,7 per cent) were clinically healthy and 18 patients (9,7 per cent) had mild symptoms.

The remaining 70 patients (37,6 per cent) had severe discomforts of their disease. 46 of them (24,7 per cent of the total material) had been operated on later for their disease; 5 (2,7 per cent of the total material) had died from gall stone disease or cancer of the gall bladder, and the remaining 19 patients (10,2 per cent of the total material) had recurrent attacks or other discomforts of gall stone disease attended by reduced state of health and capacity for work.

In order more closely to analyse the material, the cases are arranged according to the principles stated above.

In table 19, the material is analysed in regard to the state of health, at the re-examination, both of the patients who were treated for their first attack of biliary colic and of those who had had more than one attack.

Among the cases of cholelithiasis, 73,1 per cent were healthy after the first attack, and 47,5 per cent were healthy after more than one attack. The difference is statistically not probable (difference =  $25,6 \pm 11,7$ ).

Among the cases of cholecystitis, 59,1 per cent were healthy after the first attack, and 38,9 per cent were healthy after several attacks. The difference is statistically not probable (difference =  $20,2 \pm 9,0$ ).

In the total material, 63,0 per cent were healthy after one attack of biliary colic, and 42,6 per cent were healthy after more than one attack. The difference is statistically probable (diff. =  $20,4 \pm 7,2$ ).

Owing to the small number of cases, the other percentage figures given in the table for the group »mild symptoms» are of no real value.

The percentage figures for the group »severe symptoms» show that those who had had only one attack, in a smaller percentage of the cases have more severe discomforts than those who had had several attacks. The difference is statistically probable.

No obvious difference in the tendency to relapse between men and women can be discerned in the tables. The figures are mostly of the same order of magnitude.

There is thus justification for the statement that *the risk of relapse probably is smaller after the first attack of biliary colic than after several attacks.*



Tabell 19. *Re-examination of patients not operated on during first stay in hospital (exclusive of those who had died from disease other than gall stone disease).*

| Number of attacks at the<br>time of first stay in<br>hospital | Clinically healthy |       |        |       |            |       | Mild symptoms |       |        |       |            |      |
|---------------------------------------------------------------|--------------------|-------|--------|-------|------------|-------|---------------|-------|--------|-------|------------|------|
|                                                               | Men                |       | Women  |       | Both sexes |       | Men           |       | Women  |       | Both sexes |      |
|                                                               | Number             | %     | Number | %     | Number     | %     | Number        | %     | Number | %     | Number     | %    |
| <i>Cholelithiasis</i>                                         |                    |       |        |       |            |       |               |       |        |       |            |      |
| at most 1 attack .....                                        | 8                  | 72,7  | 11     | 73,3  | 19         | 73,1  | 1             | 9,1   | 2      | 13,3  | 3          | 11,5 |
| more than 1 attack....                                        | 5                  | 71,4  | 14     | 42,4  | 19         | 47,5  | 1             | 14,3  | 4      | 12,1  | 5          | 12,5 |
| diff. %                                                       | +1,3               | ±21,7 | +30,9  | ±14,3 | +25,6      | ±11,7 | -5,2          | ±15,8 | +1,2   | ±10,4 | -1,0       | ±8,2 |
| <i>Cholecystitis</i>                                          |                    |       |        |       |            |       |               |       |        |       |            |      |
| at most 1 attack .....                                        | 12                 | 60,0  | 27     | 58,7  | 39         | 59,1  | 2             | 10,0  | 3      | 6,5   | 5          | 7,6  |
| more than 1 attack....                                        | 8                  | 50,0  | 13     | 34,2  | 21         | 38,9  | —             | —     | 5      | 13,2  | 5          | 9,3  |
| diff. %                                                       | +10,0              | ±16,6 | +24,5  | ±10,6 | +20,2      | ±9,0  | +10,0         | ±6,7  | -6,7   | ±6,6  | -1,7       | ±5,1 |
| <i>Total material</i>                                         |                    |       |        |       |            |       |               |       |        |       |            |      |
| at most 1 attack .....                                        | 20                 | 64,5  | 38     | 62,3  | 58         | 63,0  | 3             | 9,7   | 5      | 8,2   | 8          | 8,7  |
| more than 1 attack....                                        | 13                 | 56,6  | 27     | 38,0  | 40         | 42,6  | 1             | 4,3   | 9      | 12,7  | 10         | 10,6 |
| diff. %                                                       | +7,9               | ±13,4 | +24,3  | ±8,5  | +20,4      | ±7,2  | +5,4          | ±6,8  | -4,5   | ±5,3  | -1,9       | ±4,3 |

Table 19 (continued).

| Number of attacks at the<br>time of first stay in<br>hospital | Severe symptoms (inclusive of those later<br>operated on and deaths from gall stone disease) |      |                  |      |                  |      | Total  |       |        |       |
|---------------------------------------------------------------|----------------------------------------------------------------------------------------------|------|------------------|------|------------------|------|--------|-------|--------|-------|
|                                                               | Men                                                                                          |      | Women            |      | Both sexes       |      | Men    |       | Women  |       |
|                                                               | Number                                                                                       | %    | Number           | %    | Number           | %    | Number | %     | Number | %     |
| <i>Cholelithiasis</i>                                         |                                                                                              |      |                  |      |                  |      |        |       |        |       |
| at most 1 attack .....                                        | 2                                                                                            | 18,2 | 2                | 13,4 | 4                | 15,4 | 11     | 100,0 | 15     | 100,0 |
| more than 1 attack ...                                        | 1                                                                                            | 14,3 | 15               | 45,5 | 16               | 40,0 | 7      | 100,0 | 33     | 100,0 |
| diff. %                                                       | +3,9 $\pm$ 17,6                                                                              |      | -32,1 $\pm$ 12,4 |      | -24,6 $\pm$ 10,5 |      |        |       |        |       |
| <i>Cholecystitis</i>                                          |                                                                                              |      |                  |      |                  |      |        |       |        |       |
| at most 1 attack .....                                        | 6                                                                                            | 30,0 | 16               | 34,8 | 22               | 33,3 | 20     | 100,0 | 45     | 100,0 |
| more than 1 attack ...                                        | 8                                                                                            | 50,0 | 20               | 52,6 | 28               | 51,8 | 16     | 100,0 | 38     | 100,0 |
| diff. %                                                       | -20,0 $\pm$ 16,2                                                                             |      | -17,8 $\pm$ 10,7 |      | -18,5 $\pm$ 8,9  |      |        |       |        |       |
| <i>Total material</i>                                         |                                                                                              |      |                  |      |                  |      |        |       |        |       |
| at most 1 attack .....                                        | 8                                                                                            | 25,8 | 18               | 29,5 | 26               | 28,3 | 31     | 100,0 | 61     | 100,0 |
| more than 1 attack ...                                        | 9                                                                                            | 39,1 | 35               | 49,3 | 44               | 46,8 | 23     | 100,0 | 71     | 100,0 |
| diff. %                                                       | -13,3 $\pm$ 12,9                                                                             |      | -19,8 $\pm$ 8,3  |      | -18,5 $\pm$ 7,0  |      |        |       |        |       |

Table 20. *Re-examination of patients not operated on during first stay in hospital (exclusive of those who had died from disease other than gall stone disease).*

| Number of attacks at the time of first stay in hospital | Clinically healthy |       |        |       |            |       | Mild symptoms |       |        |      |            |      |
|---------------------------------------------------------|--------------------|-------|--------|-------|------------|-------|---------------|-------|--------|------|------------|------|
|                                                         | Men                |       | Women  |       | Both sexes |       | Men           |       | Women  |      | Both sexes |      |
|                                                         | Number             | %     | Number | %     | Number     | %     | Number        | %     | Number | %    | Number     | %    |
| <i>Cholelithiasis</i>                                   |                    |       |        |       |            |       |               |       |        |      |            |      |
| at most 2 attacks ...                                   | 10                 | 76,9  | 16     | 69,6  | 26         | 72,2  | 1             | 7,7   | 2      | 8,7  | 3          | 8,3  |
| more than 2 attacks                                     | 3                  | 60,0  | 9      | 36,0  | 12         | 40,0  | 1             | 20,0  | 4      | 16,0 | 5          | 16,7 |
| diff. %                                                 | +16,9              | ±24,8 | +33,6  | ±13,6 | +32,2      | ±11,7 | -12,3         | ±18,0 | -7,3   | ±9,4 | -8,4       | ±8,2 |
| <i>Cholecystitis</i>                                    |                    |       |        |       |            |       |               |       |        |      |            |      |
| at most 2 attacks ...                                   | 15                 | 65,2  | 32     | 59,3  | 47         | 61,0  | 2             | 8,7   | 4      | 7,4  | 6          | 7,8  |
| more than 2 attacks                                     | 5                  | 38,5  | 8      | 26,7  | 13         | 30,2  | —             | —     | 4      | 13,3 | 4          | 9,3  |
| diff. %                                                 | +26,7              | ±16,8 | +32,6  | ±10,5 | +30,8      | ±8,9  | +8,7          | ±5,9  | -5,9   | ±7,2 | -1,5       | ±5,4 |
| <i>Total material</i>                                   |                    |       |        |       |            |       |               |       |        |      |            |      |
| at most 2 attacks ...                                   | 25                 | 69,4  | 48     | 62,3  | 73         | 64,6  | 3             | 8,3   | 6      | 7,8  | 9          | 8,0  |
| more than 2 attacks                                     | 8                  | 44,4  | 17     | 30,9  | 25         | 34,3  | 1             | 5,6   | 8      | 4,5  | 9          | 12,3 |
| diff. %                                                 | +25,0              | ±14,0 | +31,4  | ±8,3  | +30,3      | ±7,1  | +2,7          | ±7,1  | -6,7   | ±5,6 | -4,3       | ±4,6 |

Table 20 (continued)

| Number of attacks at the<br>time of first stay in<br>hospital | Severe symptoms (inclusive of those later<br>operated on and deaths from gall stone disease) |      |                  |      |                  |      | T o t a l |       |        |       |
|---------------------------------------------------------------|----------------------------------------------------------------------------------------------|------|------------------|------|------------------|------|-----------|-------|--------|-------|
|                                                               | Men                                                                                          |      | Women            |      | Both sexes       |      | Men       |       | Women  |       |
|                                                               | Number                                                                                       | %    | Number           | %    | Number           | %    | Number    | %     | Number | %     |
| <i>Cholelithiasis</i>                                         |                                                                                              |      |                  |      |                  |      |           |       |        |       |
| at most 2 attacks .....                                       | 2                                                                                            | 15,4 | 5                | 21,7 | 7                | 19,5 | 13        | 100,0 | 23     | 100,0 |
| more than 2 attacks ...                                       | 1                                                                                            | 20,0 | 12               | 48,0 | 13               | 43,3 | 5         | 100,0 | 25     | 100,0 |
| diff. %                                                       | -4,6 $\pm$ 20,5                                                                              |      | -26,3 $\pm$ 13,2 |      | -23,8 $\pm$ 11,2 |      |           |       |        |       |
| <i>Cholecystitis</i>                                          |                                                                                              |      |                  |      |                  |      |           |       |        |       |
| at most 2 attacks .....                                       | 6                                                                                            | 26,1 | 18               | 33,3 | 24               | 31,2 | 23        | 100,0 | 54     | 100,0 |
| more than 2 attacks ...                                       | 8                                                                                            | 61,5 | 18               | 60,0 | 26               | 60,5 | 13        | 100,0 | 30     | 100,0 |
| diff. %                                                       | -35,4 $\pm$ 16,3                                                                             |      | -26,7 $\pm$ 11,0 |      | -29,3 $\pm$ 9,1  |      |           |       |        |       |
| <i>Total material</i>                                         |                                                                                              |      |                  |      |                  |      |           |       |        |       |
| at most 2 attacks .....                                       | 8                                                                                            | 22,3 | 23               | 29,9 | 31               | 27,4 | 36        | 100,0 | 77     | 100,0 |
| more than 2 attacks ...                                       | 9                                                                                            | 50,0 | 30               | 54,6 | 39               | 53,4 | 18        | 100,0 | 55     | 100,0 |
| diff. %                                                       | -27,7 $\pm$ 13,7                                                                             |      | -24,7 $\pm$ 8,5  |      | -26,0 $\pm$ 7,2  |      |           |       |        |       |



However, it is necessary to proceed further and examine whether a difference is present in the risk of relapse after the first and second attacks, as compared to more than two attacks, and so forth.

In table 20 the patients who had had one or two attacks are brought together into one group, and those who had had more than 2 attacks into another group.

Among the cases of cholelithiasis, 72,2 per cent were healthy after at most 2 attacks, and 40,0 per cent were healthy after more than 2 attacks. The difference is statistically probable (diff. = 32,2 per cent  $\pm$  11,7).

Among the cases of cholecystitis, 61,0 per cent were healthy after at most 2 attacks, and 30,2 per cent were healthy after more than 2 attacks. The difference is statistically significant (diff. = 30,8  $\pm$  8,9).

In the total material, 64,6 per cent were healthy after at most 2 attacks of biliary colic, and 34,3 per cent were healthy after more than 2 attacks. The difference is statistically significant (diff. = 30,3  $\pm$  7,1).

The percentage figures for the group »severe symptoms», in this as in the previous table, show that severe discomforts occur considerably more frequently after more than 2 attacks than after at most 2 attacks. The difference is statistically not probable for the cases of cholelithiasis, but statistically significant for the cases of cholecystitis and for the total material.

No obvious difference in the tendency to relapse between men and women can be observed in this group, either: the figures are mostly of the same order of magnitude in the different groups.

The fact that the percentage of clinically healthy subjects after at most 2 attacks is of the same order of magnitude as the percentage after one attack, can only be interpreted so that the patients who have had 2 distinctly separate attacks of biliary colic have a tendency to relapse which is of the same order of magnitude as the one applying to the subjects who have had only one attack. (In table 19, those who have had 2 attacks naturally are included among those who have had more than one attack.) If we compare the group comprising 2 attacks with the group comprising more than 2 attacks, we find that the percentage of healthy subjects in the former group is 65, and in the latter 34,3. The difference is statistically probable (diff. = 30,7  $\pm$  11,8).

*The tendency to relapse after 1, or at most 2 distinctly separate, attacks of gall stone disease thus is essentially smaller than after several attacks.*

A further support of this statement may be found in a publication of life insurance statistics («Medico-Actuarial Mortality Investigation», New-York 1914). Materials of persons suffering from gall stone disease showed a higher mortality than normal materials. The results of cases with a record of two or more attacks of gall stones or hepatic colic indicate a much higher mortality than among cases with one attack. (As in these statistics no difference was made between those who had had 2, or more than 2, attacks, it is not excluded that those who had had only 2 attacks would show a mortality of the same order of magnitude as those who had had only one attack.) See table 21.

Table 21. *Quoted from Medico-Actuarial Mortality Investigation, 1914.*

| Groups                                                       | Actual Deaths | Expected Deaths | Ratio of Actual to Expected Deaths |
|--------------------------------------------------------------|---------------|-----------------|------------------------------------|
| One attack within 5 years of application .....               | 52            | 39,88           | 130 %                              |
| One attack between 5 and 10 years prior to application ..... | 40            | 30,22           | 132 %                              |
| One attack more than 10 years prior to application .....     | 44            | 34,68           | 127 %                              |
| Two or more attacks at any time...                           | 27            | 13,85           | 195 %                              |

For reasons stated above (p. 87) we were not in a position to carry the grouping of the material according to the number of attacks further than so as to comprise those who had had 1 and 2 attacks respectively. As it is of interest to know whether the rest of the material, comprising the patients who had had more than two attacks, reveals any difference in tendency to relapse between the subjects who had had a short anamnesis, and those who had had a longer anamnesis, we divide the remaining material in two fairly equal groups. One group includes the patients who had had attacks of gall stones during 2 years at most, the other those who had had attacks over a longer period than 2 years. See table 22. The percentage of healthy subjects in the former group

is 36,7, and in the latter 32,6. The difference is not statistically significant, however, not even statistically probable ( $\text{diff.} = 4,1 \pm 11,3$ ). It is possible that a larger material would be capable of giving a statistically significant difference between the percentage of healthy subjects and the tendency to relapse in these two groups, but this possibility seems to be fairly small, as our material is a comparatively large one.

*The material consequently gives no support to the assumption that the tendency to relapse for patients who have been ill during a prolonged period, would be greater than for those who have been ill during a shorter period, provided that the patient has had more than 2, distinctly separate, attacks of gall stone disease.*

If we compare the cases of cholelithiasis with those of cholecystitis we find that the percentage of healthy subjects among the former is greater than among the latter, both as regards those who had had 1, or at most 2, attacks, and as regards those who had had several attacks. The difference, however, is not statistically significant, not even statistically probable ( $\text{diff.} = 7,6 \pm 7,6$ ). It cannot be excluded that larger materials might yield figures justifying a statement as to a difference in the tendency to relapse within these different groups. Our material is too small to allow of any definite conclusion on this point, it is true, but as it comprises 66 cases of cholelithiasis and 120 cases of cholecystitis, the difference that might be obtained in a larger material at any rate cannot be of a very high order of magnitude; at most a fairly small difference can be expected.

The question arises whether the tendency to relapse is the same for patients in different age groups, or if it varies with the age of the patient. In order to get an idea of the situation, we divide the material into two groups, one comprising the cases under the age of 50, the other the cases over 50. See table 22. In the former group 51,2 per cent were healthy, and in the latter 53,9 per cent were healthy, the difference being statistically neither significant nor probable ( $\text{diff.} = 2,7 \pm 7,4$ ).

*The material accordingly seems to show that the tendency to relapse is about the same for younger and for older patients.*

It might be of interest to compare the result of our examination with the one obtained by LIEBERG for acute cholecystitis. LIEBERG's result of the re-examination of the patients not operated on

Table 22. *Re-examination of patients not operated on during first stay in hospital (exclusive of those who had died from disease other than gall stone disease). Distribution by age at first stay in hospital and duration of disease.*

| Duration of disease                                | Under 50 years     |    |               |   |                               |    | 50 years and over  |    |               |   |                               |    | All ages           |    |               |    |                               |    |
|----------------------------------------------------|--------------------|----|---------------|---|-------------------------------|----|--------------------|----|---------------|---|-------------------------------|----|--------------------|----|---------------|----|-------------------------------|----|
|                                                    | Clinically healthy |    | Mild symptoms |   | Severe symptoms <sup>1)</sup> |    | Clinically healthy |    | Mild symptoms |   | Severe symptoms <sup>1)</sup> |    | Clinically healthy |    | Mild symptoms |    | Severe symptoms <sup>1)</sup> |    |
|                                                    | M                  | W  | M             | W | M                             | W  | M                  | W  | M             | W | M                             | W  | M                  | W  | M             | W  | M                             | W  |
| At most 2 attacks .....                            | 9                  | 18 | —             | 2 | 2                             | 12 | 16                 | 30 | 3             | 4 | 6                             | 11 | 25                 | 48 | 3             | 6  | 8                             | 23 |
| More than 2 attacks during 2 years at most .....   | 3                  | 5  | —             | 1 | 1                             | 9  | 1                  | 2  | —             | — | —                             | 8  | 4                  | 7  | —             | 1  | 1                             | 17 |
| More than 2 attacks during more than 2 years ..... | 3                  | 5  | —             | 5 | 3                             | 6  | 1                  | 5  | 1             | 2 | 5                             | 7  | 4                  | 10 | 1             | 7  | 8                             | 13 |
| Total                                              | 15                 | 28 | —             | 8 | 6                             | 27 | 18                 | 37 | 4             | 6 | 11                            | 26 | 33                 | 65 | 4             | 14 | 17                            | 53 |

<sup>1)</sup> inclusive of those later operated on and deaths from gall stone disease.



is this: »Es scheint also aus diesem Material hervorzugehen, das die Aussichten in dem einzelnen Fall von akuter Cholecystitis, im weiteren Verlauf ohne Operation hinsichtlich des Gallenwegeleidens gesund zu werden bzw. zu bleiben, um so grösser sind, je kürzer die Gallenanamnese ist.« However, the figures given by LIEBERG do not fully justify the above interpretation. For the different groups of cases, with short or more prolonged anamneses, the percentage figures are given together with their standard errors for the clinically healthy subjects, but the corresponding differences with their standard errors are not stated. (See LIEBERG, p. 130).

If we calculate the differences we find that no statistically significant, or even probable, difference is present in the percentage of clinically healthy subjects among those who had had only one attack, as compared to those who had been ill between 1 and 5 years (diff. =  $17,6 \pm 9,4$ ). The relation is the same between the percentages of clinically healthy persons among those who had had attacks of gall stone between 1 and 5 years, and over a period of more than 5 years (diff. =  $5,2 \pm 9,7$ ). A statistically probable difference is present, on the other hand, between the percentages of clinically healthy persons among those who had had only one attack, and those who had had attacks of biliary colic over a period of one year or longer (diff. =  $20,6 \pm 7,4$ ). This indicates that the prognosis for those who have had one attack, is more favourable than for those who have had attacks over a more prolonged period.

We have pointed out above (p. 84) that only that part of a re-examined material of persons suffering from gall stone disease which has been under observation over a period of at least 5 years, gives fairly reliable data on the tendency to relapse. From LIEBERG's material we have sorted out the cases who were observed over a time of at least 5 years. Of 34 patients who had only had one attack of gall stone, 14 (41,2 per cent) were healthy. Of 49 patients who had had attacks over a time of at least 1 year, 8 (16,3 per cent) were healthy. The difference is statistically probable (diff. =  $24,9 \pm 9,9$ ). The material is small, and consequently it seems probable that a larger material might give a statistically significant difference in the tendency to relapse among those who had had only one attack, as compared to those who had been ill over a more prolonged period, in agreement with the results obtained in our own material.

### Summary.

During the years 1922—1935, 498 cases of gall stone disease which were not operated upon during their first stay in hospital, were treated in the surgical clinic in Uppsala. 189 patients suffered from non-complicated gall stone disease (cholelithiasis): none of these died. 309 patients presented acute cholecystitis: of these, 20 died during their stay in the hospital.

The indications for conservative treatment adopted in the clinic were as follows. The patients who came to treatment for their first attack were not operated on except on vital indication (widespread peritonitis, menacing perforation, etc.). To the patients who had had repeated attacks, operation was recommended, unless an operation was contraindicated by another disease, advanced age, and so on.

An examination of the deaths shows that the contraindications against operation, so far as may be judged, were justified: we have no plausible reasons to assume that the mortality in the material would have been lower if wider indications for operation had been applied.

A re-examination was carried out of the patients discharged from the hospital during the years 1922—1930, 216 in number. No data could be obtained on 7 patients. 28 patients had died after the stay in hospital. The state of health at the time of re-examination was analysed for the remaining 181 patients plus 5 patients who later on died from gall stone disease or cancer of the gall bladder, in all 186 patients. 98 of them (i. e. 52.7 per cent) were clinically healthy. 18 patients (i. e. 9.7 per cent) had mild discomforts. The remaining 70 patients (i. e. 37.6 per cent) had severe discomforts from their disease. 46 out of the 70 patients (i. e. 24.7 per cent of the total material) had later been operated on for their disease, 5 (i. e. 2.7 per cent of the total material) had died from gall stone disease or cancer of the gall bladder, and the remaining 19 patients (i. e. 10.2 per cent of the total material) had recurrent attacks or other severe symptoms of gall stone disease with reduced state of health and reduced capacity for work.

A close analysis of the re-examined cases shows:

that no significant difference in tendency to relapse is present between the cases of cholelithiasis and the cases of cholecystitis (a priori it is to be expected that an acute cholecystitis would result

in a greater tendency to relapse than a non-complicated attack of gall stone disease),

that the tendency to relapse after one attack of gall stone disease, whether combined with cholecystitis or not, is considerably smaller than after several attacks,

that the tendency to relapse after two, distinctly separate, attacks of gall stone disease is of the same order of magnitude as the one applying to one attack,

that, accordingly, the tendency to relapse after more than 2 attacks of gall stone disease is considerably greater than after one, or at most two, attacks.

## CHAPTER 6.

### Cases operated on.

In the surgical department of the Academical Hospital in Uppsala 620 patients were operated on for gall stone disease during the years 1922—1935. Of these, 57 had been treated in the clinic on a previous occasion for their disease but had not been operated on at that time. These 57 cases are also included in the account of the patients not operated on, given in the preceding chapter.

The material is divided into three groups according to the form of gall stone disease for which the patient was operated on:

#### I. *Non-complicated cases of gall stone disease.*

##### Cholelithiasis and chronic cholecystitis.

In this group are included both the cases in which the gall bladder on operation presented no, or little pronounced, changes, and the cases in which the wall of the gall bladder was thickened and a patho-histological diagnosis of »chronic cholecystitis» was given for some patients. In none of these latter cases was it possible, during the stay in hospital, to observe any clinical symptoms of acute cholecystitis, either in the form of increase in temperature, marked tenderness, or muscular rigidity over the region of the gall bladder. In the English and American literature, these two groups are frequently brought together under the term »chronic cholecystitis». As both the primary results of operation and the state of health at the time of re-examination proved to be on the whole identical for these two groups, we also considered it justified to bring them together into a joint group, under the heading »non-complicated cases of gall stone disease».

#### II. *Acute cholecystitis.*

This group comprises the cases which had a temperature of at least 38°C, tenderness and muscular rigidity over the region of the gall bladder, and in which, on operation, acute or subacute inflammatory changes were found in the gall bladder.



### III. *Choledocholithiasis.*

In this group are included all the cases in which stone in the common bile duct was removed at operation. In some of the cases (25), the patient also had symptoms of acute cholecystitis; these cases are also discussed in the account given of cases belonging to the preceding group.

In table 23 are given the cases operated on, distributed on age and sex and in the abovementioned groups, the deaths being stated. The table includes the total number of patients operated on for gall stone disease in the clinic during the years 1922—1935, consequently also the 57 cases who were previously treated in the clinic but were not operated on at that time. The table, however, only gives data on the age at the time of the first operation for gall stone disease, performed on the patient in question, and the result of this operation; a separate account is given, p. 199, of the operations which in a number of cases had to be performed at a subsequent stay in hospital (choledocholithotomy and so on).

## Hospital treatment.

### I. Non-complicated cases of gall stone disease.

In this group are included 261 cases, of which 175 may be classified as cases of non-complicated cholelithiasis, and 86 as chronic cholecystitis. Of the 261 cases, 5 died relative to the operation.

#### Indications for operation.

To the patients who had more than two, distinctly separate, attacks of gall stone, operation was recommended, unless contraindications against operation were present (advanced age, disease of heart or lungs, etc.).

#### Causes of death.

### I. In 3 of the cases, the cause of death was embolism or thrombosis.

1) 1634/1930. Woman, aged 58. First attack, setting in 9 days prior to admittance.

Admitted on June 11. Good general condition. Temp. 36,9°C. Moderately tender resistance over the region of the gall bladder. June 13. Chole-

Table 23. The patients operated on. Age at operation and deaths.

[illegible]

cystectomy. Narcosis. Strongly distended, adherent gall bladder, containing thick bile. Plum-sized stone in the gall bladder. — June 18. Pulmonary embolism. Trendelenburg's operation. June 19. Died.

Autopsy: pulmonary embolism; bronchopneumoniae. Field of operation normal.

2) 612/1932. Woman, aged 52. Attacks for 30 years.

Admitted on Feb. 26. Good general condition, fat. Temp. 37,3°C. A certain tenderness over the region of the gall bladder. Feb. 29. Cholecystectomy. Spinal anesthesia. Free gall bladder with thick walls, containing stones. March 8. Pulmonary embolism. March 13. Another attack of pulmonary embolism, on March 14 symptoms of cerebral embolism. March 18. Died.

Autopsy: pulmonary embolism; pulmonary infarction; bilateral bronchopneumoniae, foramen ovale apertum; encephalomalacia of the right occipital region, the left basal ganglion and the cortex of the left temporal lobe (probably caused by multiple small emboli). Field of operation normal.

3) 2802/1932. Woman, aged 63. Dyspeptic discomforts for 28 years. 3 attacks of biliary colic during the last 2 months, latest attack on the day prior to admittance.

Admitted on Nov. 2. Fairly good general condition, fat. Temp. 37,8°C. Tenderness in the epigastrium. Nov. 3. New attack: since then a temp. of about 38°C. Nov. 11. Cholecystectomy. Fibrously thickened gall bladder, containing a couple of stones. Mucous membrane normal. — Nov. 13. Jaundice, which disappeared in a few days. Nov. 23. Cerebral apoplexy. Nov. 25. Died.

Autopsy: embolism of the right middle cerebral artery; incipient encephalomalacia of the frontal and temporal lobes of the right hemisphere; mucopurulent bronchitis; subphrenic abscess. Fatty necroses in the field of operation.

II. The remaining two deaths were due to diseases not related to the gall stone disease: in one case diffuse peritonitis, developed from a septic abortion, in the other intense bleeding from a gastric ulcer.

4) 2339/1927. Woman, aged 22. First attack, setting in 5 days prior to admittance; dull pain in the epigastrium.

Admitted on Sep. 18. Good general condition, temp. 37,8°C. Tenderness over the region of the gall bladder. Sep. 26. Cholecystectomy. Narcosis. Shrivelled gall bladder with thick walls, containing a slightly turbid liquid and stones. Sep. 28. Rising temperature, symptoms of peritonitis. Re-laparotomy with incision below the navel. Pus containing streptococci in the abdomen. Oct. 1. Died.

Autopsy: fibrinopurulent pleuritis; purulent peritonitis; septic abortion. Field of operation normal.

5) B 487/1924. Man, aged 43. Two attacks over a period of 7 years. Latest attack the day before admittance.

Admitted on July 31. Slightly affected, slightly jaundiced. Temp. 38,3°C. Tenderness and rigidity over the region of the gall bladder.

Operation the same day: Cholecystectomy and closure of peptic ulcer. Fibrinous peritonitis in the upper portion of the abdomen, developed from a gastric ulcer. Small, shrivelled gall bladder, filled with stones. Aug. 3. Died.

Autopsy: fibrinous peritonitis, chronic gastric ulcer with arterial arrosion and melena.

Naturally, it is not wholly inconceivable that the issue might have been different in case 4, if the patient had not been operated on for her gall stone disease, as in that case it might perhaps have been possible to diagnose earlier the peritonitis which was the immediate cause of death. In case 5 the patient was operated on at the same time for gastric ulcer which no doubt had caused many of the clinical symptoms and from which the lethal hemorrhage emanated. The latter two deaths should in our opinion only in part be put down to the gall stone disease or the cholecystectomy. It is, however, impossible to decide to what extent the gall stone disease, or the operation for this disease, should be considered responsible for the issue in these cases, even though the chief cause of death was another disease.

If we are of the opinion that the latter two cases of death, like the other three deaths, ought to be put down to the operation for the gall stone disease, the mortality for the total material is still fairly low, 1,9 per cent. For the cases of cholelithiasis alone, with one death, it is 0.6 per cent, and for the cases of chronic cholecystitis, with 4 deaths, 4,7 per cent. The difference between the percentages of mortality in these two groups of cases is, however, not statistically significant, or even probable ( $\text{diff.} = 4,1 \pm 2,1$ ).

If we do not consider the latter two deaths to be caused by the operation for the gall stone disease, the percentage of mortality for the total material is 1,2. for the cases of cholelithiasis 0,6, and for the cases of chronic cholecystitis 2,3. The difference between the two latter figures of mortality is not statistically significant or probable ( $\text{diff.} = 1,7 \pm 1,7$ ).

The difference in mortality between cases of cholelithiasis and cases of chronic cholecystitis in the material is, as stated above, statistically not significant or even probable. This is one of the reasons why these two groups of cases were brought together into a joint group. However, the possibility is not excluded that a



larger material might show that the risk of dying after cholecystectomy is greater in cases of chronic cholecystitis than in cases of cholelithiasis; the difference in risk to be obtained in a larger material would no doubt be of a small order of magnitude, as our material is a comparatively large one.

The mortality in our material following cholecystectomy is, as stated above, comparatively small for non-complicated cases of gall stone disease. It is not greater than what is to be expected after any other abdominal operation of the same complexity.

The data on the mortality after operation for non-complicated gall stone disease to be found in the literature, present a mortality of the same order of magnitude as the one we have found in our material. Some figures from recent years are given in table 24.

Table 24. *Mortality after cholecystectomy in non-complicated cases.*

| Author                         | Number of cases | Deaths | Percentage of deaths |
|--------------------------------|-----------------|--------|----------------------|
| RINGEL and KLEINSCHMIDT 1923   | 103             | 3      | 2,9                  |
| ANSCHÜTZ 1927 .....            | 300             | 3      | 1,0                  |
| ORATOR and STRAATEN 1930 ..... | 121             | 3      | 2,48                 |
| ROWLANDS 1932 .....            | 434             | 17     | 1,62                 |
| WILKIE 1933 .....              | 528             | 11     | 2,08                 |
| FOWLER 1933 .....              | 589             | 11     | 1,87                 |
| RANZI 1934 .....               | 106             | 1      | 0,94                 |
| FINSTERER 1935 .....           | 359             | 10     | 2,78                 |
| Total                          | 2540            | 47     | 1.9                  |

In all 47 cases died of these 2540, that is to say 1,9 %, a figure which does not differ much from the one obtained in our material.

The mortality figure for our total material has a standard error ( $1,9 \pm 0,8$ , or  $1,2 \pm 0,7$ , according as the latter two deaths are included or not) which makes it possible to obtain an equally large series of cholecystectomies for non-complicated gall stone disease without a single death.

Of the 5 deaths, the first 3 were elderly patients (52, 58, and 63 years old), whereas the latter two were younger patients (22 and 43 years old).

As the mortality in the material thus is of a comparatively small order of magnitude, and as there is further the possibility that, by chance, it may equal 0, and as, finally, most of the deaths were

elderly persons, we may assert that cholecystectomy for non-complicated gall stone disease does not involve a great risk, and that, for younger patients, say under 50, it involves hardly any risk at all.

## II. Acute cholecystitis.

Before entering on a close scrutiny of the primary results of operation in our own material, we intend to give a survey of the literature on the treatment of acute cholecystitis.

In chapter I we pointed out that no far-reaching conclusions can be drawn from the early literature. The following review therefore will be mainly restricted to the time after the year 1920.

In view of the numerous statements in the literature as to the death-risk following operation for acute cholecystitis it should here be emphasized that the cases operated on constitute a selection among the patients. They consist partly of individuals who do not present too mild symptoms, but partly of individuals who do not present too severe symptoms. A person in a dying condition is not readily operated on, naturally; when it is a question of almost hopeless cases, the line of demarcation is drawn in a very different manner: some surgeons operate in order to give the patient a chance of recovery, others prefer not to operate in such cases. The proportion of severe and less severe cases further is not the same in materials from different hospitals, and often impossible to conclude from the data given on the material. Finally, only scanty information is available on the part of the material that has not been operated on, whether the patient was thought too ill for an operation to be performed with any chance of success, or an operation was avoided for other reasons (comparatively mild form of disease, advanced age, other diseases, and so forth). Neither are data as a rule given on the number of those not operated on who died of their disease.

In view of what has been said above we may assert that the materials published are hardly fully comparable.

It is of a certain interest to find out, however, whether the figures published are capable of giving information as to the magnitude of the death-risk for *all* the cases of acute cholecystitis operated on by the different authors. In many cases, data are given only for part of the material, for instance the cases on which cholecystectomy was performed, whereas other cases also operated on are reported incidentally or are brought together with other groups of cases ope-

rated on. We have made an attempt to calculate the mortality of the *total* material of cases operated on for cholecystitis in cases suited to such a calculation. The risk figures obtained in this manner must be accepted with a certain reservation for reasons stated above.

The attitude in *Germany* around the year 1920 was as follows: most surgeons supported the view expressed by KEHR in 1913 to the effect that most cases of acute cholecystitis could be treated conservatively in order later to be operated on during the interval; severe cases with marked peritoneal irritation, however, should be operated on immediately. KEHR was moreover of the opinion that only 20 per cent of all cases of gall stone disease ought to be operated on at all.

As early as 1903, however, RIEDEL advocated a divergent view, holding that cases of acute cholecystitis ought to be treated as cases of acute appendicitis, that is to say they should be operated on as soon as possible, preferably within 24 hours of the onset of the disease. RIEDEL further believed that about 90 per cent of those suffering from gall stone disease should be treated surgically.

During the years around 1920, an increasing number of authors insisted that cases of acute cholecystitis ought to be treated more actively according to the lines of treatment suggested by RIEDEL. In 1918, KIRSCHNER claimed that the high mortality following operations for gall stone disease was related to the fact that too many cases had been subjected to internal treatment over too long a period. The patients suffering from acute cholecystitis who were submitted to treatment during the first 24 hours of the disease were immediately operated on by him; those who were admitted only after a couple of days were to begin with treated conservatively in order later to be operated on, if possible, during the remission. In those cases belonging to the latter category in which the condition seemed to be menacing (risk of peritonitis or perforation, etc.), operation was immediately performed, irrespectively of the duration of the disease.

ROHDE, who in 1920 gave an account of material from the Frankfurt clinic, divided the cases of acute cholecystitis into two groups. One group, the so-called »primärentzündliche Fälle«, comprised the cases in which the inflammatory process had developed in a previously healthy gall bladder. As, in these cases, there was a

great risk of the inflammation spreading to the peritoneum (owing to deficient tendency to protecting adhesions, etc.), they were immediately operated on. In his material he had 10 such cases, operated on without fatal issue. To the second group belonged the cases in which the acute inflammation had affected a gall bladder previously chronically inflamed. As these cases were considered to involve a smaller risk of peritonitis, they were operated on immediately only if signs of complicating processes were present (gangrene, peritoneal irritation, peritonitis, perforation). The other cases were first treated conservatively, unless social indications, numerous previous attacks, jaundice in the anamnesis, or morphinism formed a relative indication for operation. As 196 cases out of 198 were operated on, relative indications for operation were apparently acted on to a large extent. 26 cases in this group were operated on on absolute indication, with 9 deaths, and 146 cases on relative indication, with 5 deaths.

In order to get an idea from ROHDE's material of the mortality in all the cases operated on, we have to add to the two abovementioned groups 24 cases operated on for acute cholecystitis, in which operation of another organ was also made (appendectomy for acute appendicitis in 16 cases, operation for pancreatitis in 4 cases, and so on). Of these cases 6 died. The total mortality for the 206 cases operated on for acute cholecystitis in the acute stage, with 20 deaths, thus is 9.7 per cent. — The division of the cases into »primärentzündliche» and other cases seems little justified. Only 10 cases could be looked upon as belonging to the former group.

In 1921, NORDMANN presented his material of cases operated on for acute cholecystitis. Starting from the view that attacks of pain in gall stone disease are due to infection of the gall bladder, he divides his material into three groups: mild cases, »cholecystitis simplex», among which are counted such cases as we have classified as non-complicated attacks of gall stones, that is to say no really acute cases of cholecystitis; medium-severe cases, and severe cases. In the mild cases operation was recommended if the patient had had one or several previous attacks. Of the 21 patients operated on, none died. In the medium-severe cases presenting destructive changes in the wall of the gall bladder, and possibly empyema, operation was immediately performed, or at the latest 15—16 days after the onset of the disease. 97 were operated on; no death occurred. In the severe cases presenting empyema in the gall bladder and peri-



tonitis, gangrenous cholecystitis, cholangitis, or pancreatitis, operation was immediately performed (16 cases, of which 4 died.) — If we are of the opinion that only the latter two groups of cases should be counted as acute cholecystitis, the mortality in NORDMANN's material is 3,5 per cent (113 patients operated on in the acute stage, with 4 deaths).

In 1921, KÖRTE in a contribution to a debate mentioned that he had operated on 265 cases of acute cholecystitis in the acute stage with a mortality of 4 per cent. In this material, however, the cases with perforation and peritonitis were not included; accordingly, the figure of mortality given must be looked upon as a minimum figure.

HEIDENHAIN (1921) held that an immediate operation should be performed in the cases in which the gall bladder was palpable and the patient had fever and severe pains. Out of 106 patients thus operated on, 15 (14,2 per cent) died; on operation during the remission 4 patients, out of 269, died (1,5 per cent). In the latter group of cases, however, were included a number of chronic and non-complicated cases.

In 1923, BLENDERMANN gave an account of material from the Greifswald clinic where patients with acute cholecystitis were operated on as early as possible and preferably during the acute attack. Of 106 patients operated on, 8 died (7,5 per cent), whereas out of 98 patients operated on during the clinical interval, 18 died (18,4 per cent). The high mortality in the latter group of cases was at least partly due to the fact that »es handelte sich bei der grossen Mehrzahl von ihnen um dekrepide, durch ihr langes Leiden äusserst geschwächte Patienten». As, further, in both groups are included cases with stone in the common bile duct and jaundice, the figures given apparently do not sufficiently justify the view, as BLENDERMANN thinks, that operation for acute cholecystitis may be performed with a smaller risk during an attack than after it.

According to RINGEL and KLEINSCHMIDT (1923), a patient suffering from really acute cholecystitis ought to be operated on as soon as possible, whether it is a case of a first attack or not. They held that in at least part of the cases of cholecystitis which recovered during conservative treatment, a later, necessary operation was rendered more difficult on account of fusions, covered perforations, abscesses, and so on, and that an operation performed under such

conditions involved a greater risk. These cases were termed »verschleppte Fälle». — After operation for ordinary acute cholecystitis, 2 patients, out of 42, died (4,8 per cent), whereas of 24 »verschläppte Fälle» operated on, no less than 5 died (20,8 per cent). The difference in mortality between these small materials is, however, not statistically probable (diff. =  $16,0 \pm 8,9$ ) and consequently the material presented by these authors is not conclusive.

KASPER (1923) presented material from the Hohenegg clinic in Vienna, where the acute cases were operated on as soon as possible. 90 cases operated on for localized acute cholecystitis showed a mortality of 3,3 per cent; 44 cases complicated by abscesses, cholangitis, etc., a mortality of 20 per cent; in all 12 deaths among 134 cases (9,0 per cent).

WALZEL stated in 1934 that in EISELBERG's clinic operations had for 3 years been performed as early as possible during the acute attack.

The investigations quoted above show that in the years around 1920, an increasing number of the surgeons in *Germany* and *Austria* began to operate on patients with acute cholecystitis during the acute stage of the disease. The figures quoted above give a general idea of the risk involved in operations of acute cholecystitis. No figures, on the other hand, are published on cases of acute cholecystitis treated in a different manner.

In *England*, where the surgeons were as a rule more conservative, cholecystostomy was performed to a large extent in cases of acute cholecystitis. SYMONDS (1924), for instance, was of the opinion that a comparison with acute appendicitis was misleading, as, in acute cholecystitis, the risk of peritonitis was considerably smaller than in appendicitis; he further thought that in most cases of acute cholecystitis it was possible to make the attack subside under conservative treatment so that operation could usually be avoided. If a case of acute cholecystitis had to be operated on, only cholecystostomy ought to be performed. A reaction against such views began to appear in the first years after 1920, however. WALTON (1923) compared acute cholecystitis to acute appendicitis and recommended immediate operation in these cases, insisting upon cholecystectomy. BLAND-SUTTON (1924) likewise preferred to perform cholecystectomy and insisted on patients with acute cholecystitis being operated on immediately and during the acute attack.

In the *United States* cholecystectomy was as a rule performed at this date. Cases of acute cholecystitis were treated conservatively as far as possible until the acute attack had subsided, in order possibly to be operated on during the remission (LYONS and JUDD, 1923).

In *France*, where cholecystostomy longest held its ground as a method of operation frequently used in gall stone disease, cholecystectomy began to be performed in acute cholecystitis in 1909 (HAUTEFORT). LERICHE and COTTE in 1912 published 7 cases operated on during the acute stage without fatal issue. LERICHE like the rest of the Lyons school subsequently (1924) claimed with energy that immediate operation should be performed in acute cholecystitis, as also CHALIER (1924) and SOUPAULT and THALHEIMER (1925). The latter authors pointed out that most French surgeons agreed at this date that cases of acute cholecystitis ought to be operated on during the acute stage, and that the debate mostly referred to the method of operation: cholecystostomy or cholecystectomy. They were themselves of the mind that cholecystectomy is to be preferred except in a far advanced cholecystitis in a very sick patient, in which case one ought to be content with cholecystostomy.

In the *Scandinavian* countries cholecystectomy had become the standard method of operation in gall stone disease, especially after the question of the method of operation had been discussed at the meeting of the Nordisk kirurgisk förening (Scandinavian Surgical Society) in Stockholm in 1911, where it turned out that a large number of surgeons had begun to adopt cholecystectomy (JOHN BERG, BORELIUS, EKEHORN, FENGERJUST, SCHOU).

The question of the treatment of acute cholecystitis was discussed at the meeting of the same Society in Gothenburg in 1916. BORELIUS, who had previously — except in cases presenting vital indication for operation — treated the cases of acute cholecystitis conservatively during the actual attack and operated only when the acute symptoms had subsided, now had begun to operate during the acute attack. BORELIUS pointed out that a gall bladder that had been the site of an actual and clear cholecystitis was changed in such a way that no doubt it had no functional value in the future and at the same time certainly rendered the patient liable to new attacks. Further, many patients could not make up their minds in favour of an operation when the acute attack had passed and

they felt all right again, while most patients without hesitation agreed to a proposed operation during the acute stage. Finally, operation in the acute stage was technically rather easier than in the chronic stage, and with satisfactory technique not essentially more risky. An adoption of early operation also carried with it the advantage that certain cases which could otherwise be treated conservatively but yet had to be operated on later, were now being operated on in an earlier stage and thus had more chances of recovery. BORELIUS's own material comprised 21 cases, operated on in the acute stage, with 5 deaths. The 5 deaths all occurred among a group of 9 patients on whom operation had to be performed on vital indications; of the other 12 cases which presented no vital indications for operation, none died.

BORELIUS's proposal was strongly supported by PAUS, who had now begun to operate in the acute stage in an increasing number of cases in order to relieve the patient once for all from his suffering and prevent a deterioration of his condition.

The situation around the year 1920 thus was this: an increasing number of surgeons, particularly in Germany and the Scandinavian countries, insisted on operation of a patient presenting acute cholecystitis, to be performed as soon as possible and preferably during the acute stage. Even the surgeons who in principle advocated expectant treatment to begin with, naturally admitted that serious cases, presenting strong peritoneal irritation, peritonitis, etc., should be operated on immediately.

At the meeting of the Deutsche Gesellschaft für Chirurgie in Berlin in 1923, HÖRZ presented a material collected from 56 German surgeons and consisting of cases of gall stone disease operated on during a period of 5 years, in all 11533 cases. On the basis of this material HÖRZ demonstrated that the postoperative mortality rapidly increased after the age of 45, and further, that the mortality of operation performed during the acute attack was almost double that of operation performed during the remission, that is to say after the acute symptoms had subsided (4761 operations during the attack with a mortality of 13,1 per cent, and 7383 operations during the remission with a mortality of 6,8 per cent).

As the material is made up of quite different operations for all kinds of gall stone disease, it is difficult, from the tables published, to infer the results of treatment for acute cholecystitis. We may



obtain a certain idea of these results by adding up the cases in which only incision for abscess was performed, those in which cholecystostomy was made, and those in which simple cholecystectomy was performed. With due reservation made for the fact that among the cases of simple cholecystectomy operated on during the interval — as also among those operated on during the attack — there no doubt are many cases operated on for »non-complicated gall stone disease», the mortality of operation for acute cholecystitis performed during the attack is 11,4 per cent (3254 operations with 371 deaths), and for operation performed during the remission, 4,5 per cent (4713 operations with 213 deaths).

HOTZ expressed the conclusions he had drawn from the investigation as follows: the patients should be recommended to subject themselves to operation in an early stage of the disease and at a less advanced age, as the mortality rapidly increases after the 45th year. Elderly persons, and particularly elderly men (the mortality for men was considerably higher than that for women), ought to be operated on only on strictly vital indications.

ENDERLEN, who at the same meeting presented his material of 728 operations for gall stone disease, demonstrated that in 332 cases, operated on at an age between 20 and 40, the mortality was 2 per cent, while it was 9 per cent for 332 cases operated on at the age of 40—60, and 17,2 per cent for 64 cases operated on between 60 and 75. ENDERLEN was of the opinion that patients ought to be operated on at the earliest possible stage of the disease, that is in early years. He coined the slogan which was later much quoted: »Frühoperation in jungen Jahren», that is to say »Frühzeitig eingreifen, sowohl in Hinsicht auf das Gallensteinleiden als auch in Hinsicht auf das Lebensalter». As operation during the stage of clinical remission involved a considerably smaller risk than operation during an attack, the acute attack should if possible be made to pass before the patient was operated on. Patients who were admitted for treatment with high temperature, distended and tender gall bladder, vomitings, considerable peritoneal irritation, suspicion of cholangitis, impending perforation, etc., were operated on immediately, however, even if it was a case of a first attack.

The views presented by ENDERLEN and HOTZ gave rise to a lively discussion, not only in Germany but also in other countries. We get a good idea of the different views which were first expressed in the

discussion by the questionnaire which the »Medizinische Klinik«, a German periodical, submitted to leading German clinicians in 1924. There were 23 answers to this questionnaire, 6 from internists, and 17 from surgeons.

The internal experts as a rule did not advocate »Frühoperation«, either in the beginning of the disease or in early years. KUTTNER thus pointed out that an acute attack is seldom directly threatening to life, that the majority of the patients passed over into a stage of latency, and finally, that operation, even when performed in early years, involved a not inconsiderable risk, as the mortality of operation performed during the remission still was about 4 per cent according to HOTZ. KUTTNER further considered that operation was absolutely indicated only in a condition threatening to life, i. e. serious forms of infectious cholecystitis, obstruction of the common bile duct, peritonitis, or perforation of the gall bladder. Relative indication for operation was present if the patient had had numerous attacks, had a chronic cholecystitis, pericholecystitis, or hydrops of the gall bladder, provided that conservative treatment had proved to be of no avail.

MATTHES and MORAWITZ advocated similar indications for operation and agreed with KUTTNER on other points as well.

UMBER even considered that the patients who had definitely recovered after operation comprised a minority of the cases operated on. Phlegmonous cholecystitis, purulent ulcerous processes in the course of a chronically relapsing cholecystitis, empyema in the gall bladder, suspicion of cancer of the gall bladder, pancreatitis and obstruction of the common bile duct constituted absolute indications for operation. In his material, comprising 771 cases, such indications were present in 4.4 per cent of the cases. As relative indications for operation UMBER mentioned chronic relapsing cholecystitis which did not heal under internal treatment so that the patient became disabled by his disease, and further the cases which for social reasons could not be treated conservatively.

VOIT advised operation if the acute attack had not passed within a few weeks, or if the patient had had many previous attacks. As a rule, an acute cholecystitis could be treated conservatively, particularly if it was a case of a first attack.

KREHL, finally, was more active: he recommended operation not only in the cases where the patient had had chills, jaundice of pro-

longed duration, impending or actual perforation, but also in cases which relapsed in spite of internal treatment, and did not want to prolong the expectant treatment too long. »Im ganzen eher operativ als nicht operativ, sogar recht operativ«.

Among the surgeons, ENDERLEN and HOTZ, on the basis of their own investigations described above, were in favour of operation during a free interval, if possible. ENDERLEN operated immediately on patients presenting chills, high fever, intense local tenderness, jaundice, etc., on other cases only after a couple of days, when the most acute symptoms had abated. HOTZ likewise operated on serious cases immediately, but preferred, if possible, to operate during the remission.

SCHMIEDEN advocated the same indications for operation, like ANSCHÜTZ, who pointed out that as a rule it was not necessary to operate at a first attack. KÜTTNER was against the principle of operating after a first attack or in early years. Serious cases were immediately operated on; cases in which vital indication for immediate operation was not present, were preferably operated on during the interval if the patient presented empyema, hydrops, or pericholecystitic abscess.

PERTHES recommended immediate operation in phlegmonous or ulcerous cholecystitis; less serious cases were preferably operated on during the remission.

DE QUERVAIN thought it wise to postpone operation for a few days in acute cholecystitis, unless signs of peritonitis forced to earlier operation. He did not consider operation in young patients to be necessary in all cases, as the disease after one or several attacks in many cases entered upon a latent stage. The more attacks in the anamnesis, the readier he was to operate.

The above opinions on the stage most suited to operation for acute cholecystitis from a surgical point of view are in good accordance with the views expressed from internal quarters as to the treatment of severe acute cases. In the subsequent discussion it was unanimously stated that serious acute cases should be operated on, preferably as early as possible. The debate was more and more focussed on the question of the stage in which mild and medium-severe cases ought to be operated on. In distinction to the internal authors, the abovementioned surgeons pointed out that a large number of the cases in which vital indication for operation was not

present, yet ought to be operated on, although preferably during the clinically free interval.

KAPPIS did not consider operation to be necessary in mild cases in which the symptoms rapidly subsided. The more severe cases in which the inflammation did not disappear in a short time, ought to be operated on, preferably within one or two days of the onset of the disease.

ROVSING, on the other hand, advocated operation (cholecystostomy) after one or two attacks, before infection had had time to develop.

MOSZKOWICZ energetically advocated early operation at a young age.

FINSTERER, whose material included comparatively few acute cases, was in favour of operation at an early stage of the disease, in elderly persons also, and stated that the disease may give slight symptoms for many years and that the first serious attack may set in only at a more advanced age.

STICH recommended operation in the acute stage if the disease had lasted 48 hours at most (after the onset of the acute attack). In other cases he preferred to operate during the remission, unless absolute indication for operation was present (peritonitis, perforation, cholangitis, etc.). He considered operation to be indicated in less severe cases as well, unless the patient refused operation.

KIESCHNER and KURTZAHN concurred in this more active line of reasoning and were of the opinion that practically every case of diagnosed gall stone disease ought to be operated on. Cases of acute cholecystitis should be operated on during the attacks.

PELS-LEUSDEN, OEHLECKER, LÄWEN, and SCHLOFFER adopted the same views. The lastmentioned writer stated, however, that as a rule it was not necessary to operate on an acute cholecystitis as promptly as on an acute appendicitis.

The discussion above reviewed shows that there were two views on the treatment of acute cholecystitis current among surgeons; one group preferred operation during the interval, but operated on severe cases of cholecystitis immediately, and considered that part of the gall stone patients did not have to subject themselves to an operation at all (ENDERLEN, HOTZ, SCHMIEDEN, ANSCHÜTZ, KÜTTNER, PERTHES, DE QUERVAIN, KAPPIS), another held that acute cases ought to be operated on as soon as possible and that gall stone patients should be operated on, unless advanced age or other



disease contra-indicated an operative intervention (ROVSING, MOSZKOWICZ, FINSTERER, STICH, KIRSCHNER and KURTZAHN, PELSLEUSDEN, OEHLECHER, LÄWEN, and SCHLOFFER).

In the subsequent discussion KIRSCHNER (1924) stated that although patients with acute cholecystitis ought to be operated on during the attack, usually it was not necessary to operate immediately but one day could very well be assigned to suitable pre-operative preparations.

KÖRTE (1924) operated on acute cases of cholecystitis, particularly in young patients, during the attack. At the same time he pointed out that the mortality was comparatively high in non-complicated cases as well, and that one had to reckon with the fact that the disease might enter upon a prolonged stage of latency. In such cases he abstained from operation to a comparatively large extent, particularly in elderly patients.

V. HABERER (1926) was of the opinion that, if possible, no operation ought to be performed during the acute seizure except on vital indication, as operation performed during the attack had a bad prognosis. In elderly patients it was wise, if operation had to be performed, only to make cholecystostomy in serious cases.

PETERMANN (1926) preferred to operate during the attack, at least in pronounced and severe cholecystitis, because he considered the risk of infectious complications from the biliary ducts and the peritoneum to be great. Of 156 cases operated on for acute cholecystitis in which the infection was limited to the gall bladder, 3 died (1.9 per cent), while out of 384 cases presenting grave acute changes, peritonitis, perforation, pancreatitis, stone in the common bile duct, etc., no less than 80 died (20 per cent). Among these latter cases were included a non-specified number of cases with stone in the common bile duct, and therefore we cannot concur in PETERMANN's opinion that the higher mortality in the latter group of cases is a proof of higher mortality in operation of neglected cases of acute cholecystitis.

Among the 384 cases, however, there were 27 cases with perforation of the gall bladder, 17 of which died after the operation. These 27 cases which must be considered as cases of severe acute cholecystitis, may be brought together with the 156 cases operated on in the acute stage; we then get 183 cases operated on for acute cholecystitis with 20 deaths, which would mean that the mortality

for the cases of acute cholecystitis in PETERMANN'S material was 10,9 per cent. This figure may be somewhat too high, as other cases later operated on for cholecystitis with lower mortality might be included in the group of 384 cases. As the mortality in this group yet was 20 per cent, the difference between the calculated mortality for operation of acute cholecystitis and the actual mortality cannot be a great one.

STICH (1927) operated during the acute attack or within 8 days at the latest. Of 206 cases thus operated on, 14 died (6,8 per cent). For operation performed during the remission, the mortality was barely 3 per cent (the number of cases is not stated).

ANSCHÜTZ (1927) defined the interval as the stage in which the patient does not have jaundice and the temperature is at most 38° C; the attack is defined as the stage in which the patient has a temperature exceeding 38° C, or jaundice, or both. He preferred to operate during the interval; among 302 operations performed during the interval (cholecystostomy and cholecystectomy), 3 deaths occurred (1,0 per cent), whereas, of 178 patients operated on during the acute stage, 15 died (8,4 per cent). These figures are quoted from the tables published by ANSCHÜTZ, the operations for stone in the common bile duct not being included (65 operations during the acute stage with 28 deaths = 43,1 per cent, and 158 operations during the interval with 5 deaths = 3,2 per cent). Of all those operated on during the remission, 460 cases, 8 died (1,7 per cent), and of all those who were operated on during the attack, 243 cases, 47 died (19,0 per cent). The mortality for operation performed during the interval was 1,6 per cent in patients under 60, and 4,4 per cent in patients over 60. The difference in mortality in younger and older patients, however, is not statistically significant (diff. =  $2,8 \pm 4,3$ ); consequently we cannot agree with the author that the material shows that operation of older patients involves a greater risk than operation of younger patients.

KLEINSCHMIDT (1928) concurs in KIRSCHNER'S opinion to the effect that operation ought to be performed during the acute attack, but not during the first 24 hours.

WOYTEK (1928) presented a material from KÜTTNER'S clinic, where operation was still preferably performed during the stage of remission, except on vital indication. Out of 26 patients operated on at an early stage, 5 died (19,2 per cent), while of 82 patients ope-

rated on during a later stage of the acute attack (i. e. on suspicion of cholangitis, in pancreatitis, etc., in spite of the temperature having decreased) 9 died (11,0 per cent). Out of 595 patients operated on during the interval, 16 died (2,7 per cent).

ORATOR and STRAATEN in 1930 published a material from v. HABERER's clinic. Among 171 operations during non-complicated attacks the mortality was 7,6 per cent (13 deaths); among 121 operations performed during the interval it was 2,5 per cent (3 deaths). The difference, however, is not statistically significant (diff. =  $5,1 \pm 2,5$ ).

FINSTERER (1935) warned against treating the acute attack conservatively, particularly in elderly persons, in whom gangrene in the gall bladder may set in without giving marked clinical symptoms. Out of 46 cases operated on during the first 2 days, 1 died (2,2 per cent); of 79 cases operated on at a later stage, 5 died (6,3 per cent).

FINSTERER's table tells us that, of 359 patients operated on during the interval, among these cases of non-complicated gall stone disease, 10 died (2,8 per cent), and out of 125 patients operated on during the acute attack, 6 died (4,8 per cent). If to the latter group are added 9 cases operated on for perforation peritonitis, a mortality is obtained for the cases operated on during the acute stage amounting to 8,2 per cent (134 operations with 11 deaths).

Among the authors here mentioned, v. HABERER, KÜTTNER, ANSCHÜTZ, WOYTEK, and ORATOR and STRAATEN preferred operation during the interval, unless vital indications for immediate operation were present, while KIRSCHNER, PETERMANN, STICH, KLEINSCHMIDT, and FINSTERER were of the opinion that cases of acute cholecystitis should be operated on during the acute attack.

In *England*, surgeons were more conservative than on the continent. In 1929, Mc NEILL LOVE published his material of acute cholecystitis. The acute symptoms were allowed to subside, if possible before the patient was subjected to operation. Of 38 patients operated on during the acute stage, 8 died (21,1 per cent), while of 43 later operations, there were 4 deaths (9,3 per cent). Moreover, 9 patients who had first been treated conservatively, had to be operated on owing to vital indications, with 3 deaths. Thus 11 patients (23,4 per cent) died among 47 operated on during the acute stage, or later on account of acute complications. 17 patients were not

operated on; none of them died. The total mortality for the operatively treated cases of acute cholecystitis is 16,7 per cent (90 cases with 15 deaths), and for all the cases, that is to say inclusive of the 17 cases not operated on, it is 14,0 per cent (107 cases with 15 deaths). The author emphasizes the considerably increased risk of an operation performed during the acute attack. A calculation of the difference between the figures of mortality for the 47 cases operated on during the acute stage and the 43 cases subsequently operated on, however, does not give a statistically significant value (diff. =  $14,1 \pm 7,6$ ).

ROWLANDS (1932) likewise subjected the patient to expectant treatment to begin with in acute cholecystitis, and readily performed cholecystostomy in acute cholecystitis. He had made cholecystostomy in 116 cases with a mortality amounting to 18,1 per cent (21 cases), and cholecystectomy in 434 cases with a mortality of 1,6 per cent (7 cases). No information is available as to the distribution of the material on cholecystitis and non-complicated cases.

WILKIE (1933) found a high mortality in operations performed during the acute stage. Of 528 cases of cholecystectomy, 11 died (2,1 per cent). The distribution of the material on acute and chronic cases is not given.

In the *United States*, most of the surgeons around the year 1923 were of the opinion that if possible, expectant treatment ought to be tried in cases of acute cholecystitis. Gradually, and to a great extent because of the more active tendencies in Germany, some American authors also advocated active therapy during an early stage of acute cholecystitis.

BUNTS (1925) preferred to perform cholecystostomy in cases of acute cholecystitis which had to be operated on. Out of 129 such cases, 9 died (7,0 per cent). Of 400 cases of cholecystectomy, 7 died (1,8 per cent); part of them had before been subjected to cholecystostomy.

DEAVER and BURDEN (1926) emphasized the small risk of acute perforation in acute cholecystitis, and operated only when the acute symptoms had subsided.

CAVE published his material of 575 operations in 1926. Patients with acute cholecystitis were to begin with treated conservatively; if the symptoms had not essentially abated after 36 hours, cholecystostomy was performed. 105 cholecystostomies had been per-



formed with a mortality amounting to 4,8 (5 deaths), and 470 cholecystectomies with a mortality of 6,4 per cent (30 deaths). In 54 cases in which cholecystectomy was performed, choledochotomy was also made. As the material is not analysed in detail, it does not permit of any definite conclusions as to the results of the operative treatment of acute cholecystitis, although it seems probable that the majority of the 105 cholecystostomies were made for acute cholecystitis.

JUDD and PARKER (1926) during the acute stage had operated on 36 cases of acute cholecystitis with 2 deaths (cholecystostomy had been performed in 10 cases; the 2 deaths occurred after cholecystostomy). In their material, the cases of acute cholecystitis were not frequent.

DAVIS (1928) pointed out that patients suffering from acute cholecystitis ought not to be operated on immediately but should be examined and prepared at least for 2 days (kidney function test, examination of heart etc.; cardiac stimulants, supply of liquid, etc.). Of 160 cases operated on, 6 died (3,8 per cent.). The number of acute cases is not stated.

The authors mentioned above were comparatively reluctant to operate for acute cholecystitis during the acute attack.

In recent years, a number of writers have advocated a more active line of treatment.

MILLER (1930), who had 2 cases of acute cholecystitis in which the gall bladder had perforated during conservative treatment, claimed that cases of acute cholecystitis should be operated on at an early stage and during the acute attack. Of 200 acute cases operated on, 27 died (13,5 per cent.); the period elapsing between the acute onset of the disease and the operation was on an average 15 days for the 27 deaths, but 8,3 days for the successful operations.

GRAHAM (1931), who likewise insisted on early operation during the acute attack, had operated on 20 cases of acute cholecystitis within 48 hours after the acute attack and with only one death (5 per cent); of 178 cases which had been operated on at a later stage of the disease (< 2 days), 11 died (6,2 per cent). The difference, however, is not statistically probable (diff. =  $1,2 \pm 5,21$ ), and consequently we cannot draw any conclusions from the material as to the suitable time for cases of acute cholecystitis to be operated on.

ZINNINGER (1932) operated immediately on serious cases and cases

whose symptoms did not markedly subside after a few hours. He found in his material that in  $\frac{2}{3}$  of the cases, the acute symptoms did not abate but grew even worse. 35 cases were operated on immediately after the admittance to hospital: of 12 cases, which were operated on within the first 48 hours of the disease, none died; among 15 cases, which were operated on after the disease had lasted for 2—5 days, one death occurred, and of 8 cases which had been ill for more than 5 days, 2 died. The mortality in the 35 cases thus was 8,6 per cent. 54 cases were operated on only some time after the admittance to hospital. Of 18 cases which were operated on within the first week in hospital, one died, and of 36 cases which were operated on during a later stage of the disease, 3 died. The mortality for the 54 cases accordingly was 7,4 per cent. No statistical difference in mortality between the cases which were operated on immediately after the admittance to hospital and those which were operated on later, appears in ZINNINGER's material (diff. =  $1,2 \pm 5,91$ ).

MENZER (1932) had a large number of perforations of inflamed gall bladder in his material. Of 63 cases not operated on, 14 died (4 of these owing to perforation of the gall bladder; in 134 cases in all of acute cholecystitis, perforation of the gall bladder occurred in 10 cases).

FOWLER (1933) had performed cholecystostomy for acute cholecystitis in the acute stage in 235 cases with a mortality amounting to 12,8 per cent (30 deaths), and cholecystectomy in 278 cases with a mortality of 6,5 per cent. The patients suffering from acute cholecystitis in whom the acute symptoms did not rapidly subside, were operated on. If an immediate operation was not necessary, the operation ought to be postponed at least for 6 weeks.

TOUROFF (1934) stated that the patho-anatomical changes in the gall bladder may remain, or even progress, in spite of the clinical symptoms having abated. He emphasized the difficulty of making a prognosis for the attack in the separate cases and therefore advised operation if the acute symptoms do not subside rapidly and quietly.

TAYLOR (1936) had operated on 129 cases of acute cholecystitis. Out of 19 patients operated on during the first 2 days of the disease, one died; of 20 patients who were operated on during the 3rd—4th day of the disease, one died, and of 63 cases operated on during a later stage of the disease, 14 died (22,2 per cent). We have calculated the difference in mortality between the 39 cases operated

on during the first 4 days of the disease and the 63 cases later operated on and found it to be statistically probable (diff. =  $17,1 \pm 6,3$ ); TAYLOR's material thus may be adduced in support of the view that operation during an early stage of acute cholecystitis involves a smaller risk than operation during a later stage. It is worthy of notice, however, that the mortality in his total material of operations for acute cholecystitis is unusually high (15,9 per cent), which might indicate that the patients were on the whole admitted in a poor general condition.

Other writers in recent years are of the opinion that, if possible, operation should be avoided during the acute stage.

SHERWOOD (1928), who preferred to operate during the interval, had a mortality amounting to 11,1 per cent among 54 cases operated on during the acute stage (6 deaths), but only to 4,8 per cent among 146 cases operated on during the remission (7 deaths). The difference in mortality is, however, not statistically probable (diff. =  $6,3 \pm 4,6$ ), and consequently we cannot consider his figures as conclusive.

SMITH (1933) likewise operated only on vital indication during the acute stage. Of 107 operations during the acute stage, there were 10 deaths (9,3 per cent), and of 94 operations during a later stage, 5 deaths occurred (5,3 per cent). The difference in mortality, however, is not statistically probable (diff. =  $4,0 \pm 3,6$ ); the material published consequently does not allow of any conclusions as to difference in risk at operation for acute cholecystitis during one or the other stage.

BEHREND (1934) does not think that the danger of a spreading of the infection under conservative treatment is sufficiently great to justify an operation during the acute stage.

BASS and BIRD (1936) were also of the mind that cases of acute cholecystitis should not be operated on immediately but only a few days after the acute attack, and think that the majority of the cases of acute cholecystitis spontaneously recover.

BRANCH and ZOLLINGER (1936) operate only when the acute symptoms have subsided and think that this line of treatment gives the best prognosis.

WILSON, LEHMAN and GOODWIN (1936) have compared their own material of cases of acute cholecystitis, operated on within and after 48 hours, with similar data from the literature, and arrived at

the conclusion that no statistical difference can be demonstrated in the mortality for these two groups of cases. These authors are the only ones, among those so far reviewed that have treated their material from a statistical point of view.

The papers published in the United States on the treatment of acute cholecystitis, reviewed above, no more than the ones previously mentioned, give any conclusive figures. The high mortality found by one author after operation during the acute stage, is by another found after operation performed during the subsequent course of the disease. Only one writer (TAYLOR) presents figures which might support his views, but as the information on the material is otherwise sparse, too definite conclusions no doubt cannot be drawn from his material.

In the *Scandinavian* countries the treatment of acute cholecystitis was discussed at a meeting of the Danish Surgical Association in 1927. KJAERGAARD who opened the discussion, pointed out that an expectant treatment did not involve such a great risk that on this account one had to operate during the acute stage without vital indication. In his opinion the best course was to operate on the patient only when 8 days, or even more, had elapsed after the acute attack had passed. KJAERGAARD's material consisted of 116 cases of acute cholecystitis (with a temperature  $> 38,1^{\circ}\text{C}$ ; in 64 of these cases  $> 39^{\circ}\text{C}$ ). 4 of the patients had been operated on during the acute attack, with 3 deaths; 3 patients had been operated on later, as the temperature did not decrease; all three died. The other patients were either operated on during a stage without increased temperature, or not operated on at all; none of them died. The mortality in KJAERGAARD's material of acute cholecystitis consequently is 5,2 per cent (6 deaths among 116). WESSEL and FOGH-ANDERSEN were of the same mind: if possible, they avoided operation during the acute stage. Among WESSEL's 237 patients, operated on or not operated on, 25 died (10,5 per cent). FOGH-ANDERSEN presented 151 cases of acute cholecystitis, of which only 2 were operated on during the acute stage and both for the reason that the diagnosis was uncertain; none of them died. 128 patients were operated on during the remission (2 deaths), and 21 patients were not operated on (5 deaths). The mortality of the total material of acute cholecystitis was 4,6 per cent (7 deaths among 151



cases). SCHALDEMOSE and COLLIN had begun to operate during the acute attack, mostly for the reason that they considered the risk of deterioration, or even perforation, to be comparatively great during the expectant treatment. COLLIN had operated on 119 acute cases (with 3 deaths) on relative indication. Those were cases in which he thought he could choose between operation and expectant treatment. 31 patients were operated on on vital indications, with 12 deaths. The total mortality for the treated cases of acute cholecystitis accordingly was 10 per cent (150 cases with 15 deaths). PETRÉN was of the opinion that patients suffering from acute cholecystitis ought to be operated on as early as possible during the acute attack, unless general contra-indications (advanced age, diseases of heart or lungs, and so on) justified a conservative treatment, if possible. Among PETRÉN's 226 patients with acute cholecystitis, 65 had not been operated on (no death), and 161 had been operated on (20 deaths). The mortality for the total material of acute cholecystitis was consequently 8,8 per cent.

TENGVAL published his material of gall stone disease in 1930. 312 patients had acute cholecystitis. 173 among them had a temperature of at least 38°C. 22 patients were immediately operated on on vital indication, with 6 deaths. 153 were operated on the day after the admittance, with 12 deaths, and 70 on the third day, with 4 deaths. Of the 245 patients operated on within 3 days of the admittance to hospital, 22 died (9,0 per cent). TENGVAL considered it most suitable to operate after a few days had elapsed following the patient's admittance to hospital and when the most acute symptoms had subsided.

MÖLLER (1930), on the other hand, was more inclined to early operation in order to avoid having to operate under less favourable conditions at a later stage of the disease, if the patient grew worse.

At the meeting of the Scandinavian Surgical Association in Helsingfors in 1931, the indications for, and the results of, a surgical treatment of the gall stone disease were discussed. KJAERGAARD, one of the openers of the discussion, advocated the same line of treatment as in 1927 (see above), while KROGIUS, the other opener, was in favour of early operation in all fairly severe cases of cholecystitis.

In 1937, LIEBERG published a clinical study of acute cholecystitis from the surgical clinic at Lund. The material on which his investi-

gation was based comprised 556 patients both operated and not operated on. The paper which contains a detailed study of the material is by far the most thorough examination made in this field and we shall return to it below. In this connection we only note that 308 patients were operated on, with 35 deaths (11.4 per cent). As regards cholecystectomy, the percentage of mortality for the cases (93 in number) in which cholecystectomy was performed during the first 3 days of the disease, was 5.4 per cent. For the cases (75) in which the same operation had been performed during the fourth to the seventh day the mortality was 12 per cent. During the first week of the disease, 24 patients had further been subjected to another operation (cholecystostomy, incision of abscess, etc.); of these, 15 died. LIEBERG inferred from his study that serious cases of acute cholecystitis should be operated on immediately, irrespective of the day on which they come to treatment; that patients who come to treatment during the first 2 or 3 days of the disease, ought to be operated on immediately; and that patients who come to treatment later on, should be operated on at once if they present any at all alarming symptoms, or if the case is not altogether clear.

The review of the literature shows that as regards the treatment of acute cholecystitis, everybody is agreed on one point only: grave cases with pronounced peritoneal irritation, perforation, and so on, ought to be operated on immediately, unless the patient is in a condition to make all treatment of no avail. Regarding the treatment of not too severe cases, three opinions have been advanced. Some writers think that such cases should also be operated on immediately and during the acute stage. Other authors consider it advisable to postpone operation until the most acute symptoms have improved after a few days. Other surgeons again prefer to operate on such cases when the acute symptoms have subsided, when the abdominal tenderness has disappeared, when the temperature has decreased, and so forth. Individual writers from a theoretical point of view consider it most adequate not to operate until the morbid process has healed, but as this would mean that operation could not be performed until after weeks or months, this attitude is not adhered to in practice. As BORELIUS pointed out as early as 1916, it is not very probable that the patients would of their own accord subject themselves to an operation during the true interval after being discharged from hospital when the acute symptoms had improved. By operation



during the interval is generally meant operation during the stage when the clinical symptoms of the acute process have subsided, that is to say one, or maybe two, weeks after the onset of the acute attack.

Although most authors are of the opinion that, when operating on a patient for acute cholecystitis, one ought to perform cholecystectomy, there are still many who advocate cholecystostomy in acute cases, and this not only when the patient's poor general condition contra-indicates all but the least complicated operation.

The opinions reviewed in the survey of the literature are based partly on general experience, partly on series of figures. In the previous pages we have in many cases been able to show that the figures published do not justify the conclusions drawn. The larger series of figures have been brought together in table 25.

The first column includes operations during the acute attack. This group comprises all the cases of acute cholecystitis operated on during the acute stage, irrespectively of the method of operation employed, in so far as these cases can be brought together from the material of figures published. In this group are thus also found the serious cases in which it was only possible to perform cholecystostomy or incision of abscess. Under the heading »acute cholecystitis, operation during interval» were brought together the cases on which definite data were available to show that they were cases of acute cholecystitis operated on during the interval. In column 3 are entered the results of treatment for all cases of acute cholecystitis, operated on and not operated on. In by far the majority of cases, the authors in question have brought the cases of acute cholecystitis which were operated on during the interval together with the other cases of gall stone disease which were operated on during the interval. These cases are accounted for in column 4. In column 5, incisions of the common bile duct are entered, whether the operation was performed during the acute attack or during the remission. Under the heading »other operations», other cases not described in detail were entered. The last column gives information on the size of the total material in the cases in which data are given on a total material of operations for gall stone disease. Re-operations, operations of anastomosis, and operations for cancer of the gall bladder or the biliary ducts were not included in the table in so far as it was possible to separate these operations from the material of operations.



An examination of the table shows that the total mortality for cases of acute cholecystitis operated on during the acute stage presents a comparatively good accordance. The lowest mortality is found with STICH, KASPER and FINSTERER who advocate the active line of treatment, and with ANSCHÜTZ who prefers to operate during the interval; the highest mortality is to be found with HEIDENHAIN who advocates operation during the attack, and with WOYTEK who favours operation during the interval. The authors who operate during the interval have fairly unequal figures of mortality for the part of the material which does not include the gravest cases (from 1,7 up to 7,4 per cent). Information as to the number of cases of acute cholecystitis, operated on during the interval, is lacking in the majority of cases; cases presenting non-complicated gall stone disease (cholelithiasis, chronic cholecystitis) are as a rule also included. As the latter cases in our material have a mortality amounting to 1,9 per cent (see p. 105), and the data included in the table on the mortality after operation during the interval (in col. 4) are of the same order of magnitude, it is to be supposed that operation for acute cholecystitis during the interval would have a mortality of similar order of magnitude. The conclusion to be drawn from the data given in the literature would be this: it is of the greatest importance that as many as possible of the cases of acute cholecystitis should reach the stage of remission before they are operated on. On the other hand it is evident that the nature of the actual material of cholecystitis is of the greatest significance to an evaluation of the result of the treatment.

A material comprising a comparatively great percentage of far advanced cases, or many elderly patients, naturally gives a higher mortality than a material of early cases and younger patients. In most cases it is impossible to appraise in detail the nature of the materials published. It should be pointed out, however, that ROHDE stated that 26 out of the 206 patients operated on during the acute stage presented peritonitis or sepsis, that PETERMANN's material comprised 384 serious cases with peritonitis, stone in the common bile duct, abscess of the liver, etc. (with a mortality of 20 per cent), that ANSCHÜTZ's material included 60 (out of 601) patients over 60 years old and, in spite of his conservative attitude, he had to operate on 243 out of 703 cases during the acute attack (operations for stone in the common bile duct attended by chol-

angitis, etc., included), and that FINSTERER classified 21 among his 601 cases as very serious cases (perforation, severe pancreatitis, and so on).

We get the impression that PETERMANN's material includes a comparatively large number of serious cases, as also that of ANSCHÜTZ, but that in FINSTERER's material the serious cases were not equally numerous. Such an estimate of the different materials, however, necessarily is fairly rough although it may perhaps be of a certain value in judging the results of the treatment.

As yet there exists only one large investigation (published by LIEBERG in 1937) treating a total material of acute cholecystitis. The other data from the literature quoted above refer either to larger or smaller series of operations or else, in some cases, to total materials of acute cholecystitis, operated and not operated on. These latter materials (presented by KJAERGAARD, WESSEL, and FOGH-ANDERSEN) are not large but certainly give a better conception of the death-risk in acute cholecystitis than the materials which only consist of cases operated on.

We have above (in chapter 5) treated the cases of acute cholecystitis not operated on in our own material. Below we intend to treat the cases which were operated on.

#### Indications for operation.

The patients who were admitted to the hospital for their first attack of cholecystitis were as a rule not operated on, unless the cholecystitis was so advanced that it was considered advisable to operate on vital indication. To the patients who had had several attacks operation was recommended, unless general contra-indications against operation were present (advanced age, heart and vessel disease, etc.).

During the years 1922—35, 257 patients were operated on for acute cholecystitis; 27 of them died relative to the operation. Of the 257 cases, 20 had previously been treated in the clinic for gall stone disease, but had not been operated on then; among these, one died.<sup>1)</sup>

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<sup>1)</sup> These 20 cases are also included in the account of the patients not operated on, in chapter 5.

**Causes of death.****I. Embolism, 6 cases.**

1) C 102/1923. Woman, aged 58. Repeated attacks over a period of 36 years. Latest attack the day before admittance.

Admitted on Feb. 3. Slightly affected. Temp. 38,5°C. Slightly tender tumour, of the size of a goose-egg, at the site of the gall bladder. Feb. 2. Temp. 39°C. Feb. 5. *Cholecystectomy*. In the peritoneum a thin, turbid liquid. Fibrinous peritonitis round the gall bladder which was heavily distended and covered by fibrin, and contained thick pus. Abundance of stones; thick, strongly flushed mucous membrane. Feb. 11. Pulmonary embolism. Died.

Autopsy: embolism of the pulmonary artery. Field of operation presents nothing remarkable.

2) A 817/1924. Man, aged 36. Some attacks for one year and a half; latest attack the day before admittance.

Admitted on Oct. 14. Good general condition, slightly jaundiced. Temp. 38,8°C. Slight rigidity and tenderness over the region of the gall bladder. Oct. 16. *Cholecystectomy*. Heavily distended, bluish red, fibrin-covered gall bladder containing slimy liquid without bacteria. Gangrenous gall bladder in which were found numerous stones. Oct. 21. Pulmonary embolism. Trendelenburg's operation. Died.

Autopsy: thrombosis of the left hypogastric vein, pulmonary embolism. Field of operation normal.

3) 557/1926. Woman, aged 63. First attack, setting in 3 days prior to admittance.

Admitted on Feb. 17. Fairly fat, temp. 38,6°C. Marked tenderness and rigidity over the region of the gall bladder. Immediate *cholecystectomy*. Bile-coloured, slightly turbid liquid in the abdomen. Round the gall bladder purulent fibrin clots. Totally gangrenous gall bladder; a couple of stones. After a temporary decrease in temperature there was a rise up to 40°C after 3 days. March 7. Died.

Autopsy: pulmonary embolism, pulmonary infarction and bronchopneumoniae.

4) 2889/1927. Woman, aged 45. Repeated attacks for 10 years. During the last week attacks accompanied by chills.

Admitted on Nov. 23. Good general condition, temp. 38,5°C. Marked tenderness over the region of the gall bladder. Dec. 2. *Cholecystectomy*. Chronic cholecystitis with acute exacerbation. Some 50 stones. Dec. 8. Pain on the left side. Dec. 13. Pulmonary embolism. Trendelenburg's operation. Dec. 14. Died.

Autopsy: pulmonary embolism with thrombosis and incipient bronchopneumonia. Field of operation normal.

5) 485/1933. Woman, aged 60. First attack, setting in the day before admittance.

Admitted on Feb. 13. Temp. 38,6°C. Tenderness, rigidity, and resistance over the region of the gall bladder. During the 15 days elapsing between

the admittance to hospital and the performance of the operation, the patient had 3 attacks of biliary colic attended by an increase in temperature up to 39,3°C and slight jaundice. March 1. *Cholecystectomy*. Local anesthesia, 35 gm. of ether. Gall bladder of the size of a goose-egg, containing thin pus. Gangrenous cholecystitis. 10 pea-sized stones. March 6. Pulmonary embolism. March 17. Died.

Autopsy: pulmonary embolism with infarction of the right lung and bronchopneumoniae, thrombosis of the left hypogastric vein. Field of operation normal.

6) 994/1934. Woman, aged 52. Repeated attacks of gall stones for 5 years. Latest attack the day before admittance.

Admitted on March 20. Good general condition, temp. 40,4°C. Tenderness and rigidity over the region of the gall bladder. After the temperature had become normal, *cholecystectomy* was performed on March 29 (9 days following the admittance). The strongly thickened gall bladder contained purulent liquid with rods and cocci and plenty of stones. On March 30, the day after the operation, the patient died from pulmonary embolism.

Autopsy: pulmonary and cardiac embolism. Field of operation normal.

## II. Pulmonary complications, 7 cases.

7) A 93/1922. Woman, aged 46. Isolated attacks for 15 years. Latest attack several days prior to admittance.

Admitted on Feb. 3. Fairly good general condition, temp. 38,5°C. Tenderness and palpable tumour over the region of the gall bladder. Feb. 14. *Cholecystectomy*. Heavily thickened gall bladder with considerably brittle wall, containing several stones. In the common bile duct very turbid, almost pus-resembling, liquid. Feb. 16. Temp. 40,7°C. Pneumonia of the right lung. Feb. 20. Died.

Autopsy: purulent bronchitis, diffuse bronchopneumoniae. Field of operation normal.

8) B 264/1922. Man, aged 66. 3 attacks during a period of 3 years. Latest attack 11 days previously.

Admitted on April 29. General condition affected. Temp. 38,6°C. Slightly jaundiced. Basal bronchitis. Fist-sized, somewhat tender resistance over the region of the gall bladder. At first decreasing temperature and improved abdominal symptoms. May 3. Increasing temp. and increased symptoms. May 3. *Cholecystectomy*. Local anesthesia, 60 gm. of ether. Gangrenous cholecystitis with thick pus in the gall bladder, smelling of coli. May 6. Pneumonia of the right lung. May 7. Died.

Autopsy: bronchopneumoniae, well circumscribed, subphrenic abscess of the right side. Field of operation normal.

9) C 331/1924. Man, aged 73. 2 attacks in one month and a half. Latest attack set in during stay in hospital for pleural empyema. From March 21 to April 17 treated for chronic ileus of the small intestine and colitis? Admitted on account of pains in the upper portion of the abdomen. Temp. 37,8°C. Diffuse tenderness in the right upper part of the abdomen. — Again admitted



on May 15 for abscess of the prostate. July 5. Empyema of the right pleura. Aug. 13. Resection of the ribs, thoracotomy, drainage. Dec. 5. Acute attack attended by pains in the right upper portion of the abdomen. Extremely strong rigidity, pronounced tenderness on pressure over the region of the gall bladder. Immediate operation: *Cholecystostomy*. Fibrinous peritonitis in the upper part of the abdomen, most pronounced round the gall bladder which had thick walls and contained a large stone and light grey, turbid liquid. Dec. 6. Died.

Autopsy: chronic bilateral adhesive pleuritis, lobar pneumonia of the left lung; acute circumscribed peritonitis, acute ulcerous cholecystitis, acute nephritis.

10) 1167/1925. Woman, aged 30. Had had 2 attacks of biliary colic over a period of one month. Latest attack 3 days prior to admittance.

Admitted on May 17. Slightly affected. Temp. 39,4°C. Circumscribed tenderness over the region of the gall bladder. The temperature gradually decreased to 38,4°C. May 20. *Cholecystectomy*. Narcosis. Fibrin-covered, fist-sized gall bladder, containing purulent liquid. The wall of the gall bladder was phlegmonous. In the gall bladder numerous stones. Died the day after the operation, increase of temperature up to 43°C.

Autopsy: fatty heart; fibrous myocarditis, inflammatory pulmonary edema. Field of operation normal.

11) 1511/1928. Woman, aged 75. First attack, setting in the day prior to admittance.

Admitted on May 31. Affected, fat, slightly icteric. Tenderness and rigidity in the upper right portion of the abdomen. Immediate *cholecystectomy*. Local anesthesia, narcosis. Heavily distended gall bladder containing turbid liquid with an abundant amount of bacteria. The wall of the gall bladder inflamed. In the gall bladder some 80 stones. June 6. Cough. June 7. The wound ripped open. June 10. Died.

Autopsy: acute endocarditis; acute bronchopneumoniae; circumscribed fibrinous peritonitis.

12) 2106/1928. Man, aged 76. First attack 2 years previously. Second attack on the day of admittance.

Admitted Aug. 7. Slightly affected, senile, arteriosclerotic. Temp. 38,1°C. Tenderness and rigidity below both right and left arch. Aug. 7. X-ray examination revealed acute pancreatitis. Aug. 8. Rising temp. and deteriorated general condition. Jaundice. Strongly increased peritoneal irritation. *Cholecystectomy*. Large quantities of turbid, somewhat bile-coloured liquid in the upper portion of the abdomen. Totally gangrenous gall bladder, containing coli, bile, and several stones. The pancreas markedly thickened. No fatty necroses. Aug. 13. Double-sided pneumonia. Aug. 14. Died.

Autopsy: exudative, hemorrhagic pleurisy; acute mucopurulent tracheo-bronchitis; bronchopneumoniae; circumscribed peritonitis.

13) 419/1930. Woman, aged 50. Several attacks for 28 years. Latest attack 2 days prior to admittance.

Admitted on Feb. 4. Fairly satisfactory general condition. Very fat. Temp. 37,8°C. Slight tenderness below the right arch. Feb. 8. Chill attended by

a temp. of 40,5°C. Feb. 15. Acute pains in the region of the gall bladder. Temp. 39,6°C. Feb. 21. The temperature has gradually decreased to 38,2°C. *Cholecystectomy*. Considerably enlarged liver. Shrivelled gall bladder, perforated to an abscess, the size of a walnut, containing 2 stones. Feb. 28. The temp. after the operation between 38° and 39°C. New chill, followed by a temp. of 39,4°C. In the wound abundance of necrotic tissue. March 3. Rapidly deteriorated general state of health. Bronchopneumonia of the left side. Died.

Autopsy: bronchopneumonia; hemorrhagic pleurisy of the right side; hepatic abscess.

In two of these cases, to judge from the histories of disease, the pulmonary disease does not seem to have been the sole cause of death. In case 8, the patient, in addition to bronchopneumonia of the right side, also presented a right-sided subphrenic abscess. As the latter, however, seems to have been well circumscribed and as the patient further showed symptoms of basal bronchitis even at the admittance to the hospital (4 days prior to the operation), we believe that the pneumonia must be looked upon as the principal cause of death. In case 13, an abscess was found in the liver at the operation, relative to the abscess developed from the gall bladder which was also found at the operation. As, however, the post-mortem examination showed considerable changes both in the lungs and the right pleura, it seems to us most probable that both the rise in temperature after the operation and the death were caused by these changes; consequently we have included this case among the deaths from complications of the lungs. In case 10 it should be noted that it is possible that operation was performed at a too early stage: the morbid process was not very advanced and the patient died of a very acute pneumonia attended by hyperthermia. The operation which was performed under narcosis the day before the patient died, in this case no doubt greatly influenced the rapid course and fatal issue of the pulmonary affection.

### III. Other disease, 2 cases.

14) B 601/1923. Woman, aged 50. Several attacks over a period of 8 years. Latest attack the day before admittance.

Admitted on Oct. 26. Very fat. Temp. 37,9°C. Moderately tender tumour at the site of the gall bladder. Oct. 31. The temperature kept between 38° and 39°C. To-day mild attacks, mild jaundice. Nov. 1. *Cholecystectomy*. Strongly distended gall bladder, containing purulent liquid. Numerous stones. Nov. 12. Rising temp. From the wound abundant quantities of odourless

gas. *Re-laparotomy*. Purulent pelvic peritonitis, probably developed from a gangrenous appendicitis. Nov. 13. Died.

Autopsy: appendicitis-peritonitis.

In this case the patient died from a peritonitis developed from the appendix. It might be imagined that the fact that the patient had recently been operated on for cholecystitis to a certain extent had caused the appendicitis not to be diagnosed in time. As, however, 11 days had elapsed between the cholecystectomy and the symptoms of peritonitis, this assumption does not seem to us very probable. Another possibility is that the appendix was inflamed already at the time of the cholecystectomy and that the peritonitis took a lingering course until it gave symptoms comparatively quickly.

15) B 647/1924. Man, aged 68. Attacks for 5 years. Latest attack 2 days prior to admittance.

Admitted on Sep. 15. Affected. Cyanotic, slightly jaundiced. Temp. 39,4°C. Rigidity and marked tenderness over the region of the gall bladder. — The same day *cholecystectomy*. Local anesthesia, narcosis. The gall bladder was heavily distended and totally gangrenous, containing purulent liquid and some 20 stones. Sep. 17. Quantity of urine 50 c.c. Sep. 22. Quantities of urine between 50—120 c.c. per 24 hours. Temp. 36,6°C. The patient confused. Sep. 24. Died in a state of coma.

Autopsy: myocarditis; circumscribed peritonitis; acute pyelonephritis. Microscopic examination: acute diffuse glomerulonephritis.

#### IV. The cholecystitis. 12 cases.

In 3 cases the cholecystitis was restricted to the gall bladder.

16) 445/1926. Woman, aged 42. 2 attacks over 1 year. Latest attack 2 days prior to admittance.

Admitted on Feb. 4. Good general condition, fat. Temp. 38,4°C. Moderate tenderness over the gall bladder. Feb. 8. Jaundiced, feces greyish white. Feb. 11. *Cholecystectomy, choledochotomy*. The walls of the gall bladder somewhat thick. The bladder contained one stone; the common bile duct had thick walls, tough. No obstruction could be observed in the common bile duct. Rising temperature after the operation. Feb. 20. Died.

No autopsy.

17) 1491/1929. Woman, aged 62. Several attacks of gall stones in the anamnesis. Latest attack 3 days prior to admittance.

Admitted on June 26. Affected general condition; slightly jaundiced, temp. 38,7°C. Resistance, tenderness and rigidity over the region of the gall bladder. The temp. decreased in the course of the day and on account of this, expectant treatment was decided on. June 13. Chill, heart collapse. Temp.

40,1°C. The condition improved somewhat after strong stimulation, but deteriorated again with increase of temp. to 41,3°C. *Cholecystostomy*. Large gall bladder, containing pure pus, microscopically without bacteria. Died a few hours after the operation.

No autopsy.

18) 1683/1931. Woman, aged 61. Isolated attacks for 25 years; latest attack the day before admittance.

Admitted on July 1. Affected general condition. Very fat. Temp. 39,8°C. Marked tenderness and rigidity over the region of the gall bladder. July 2. Temp. 38,8°C. *Cholecystectomy*. Free edematous gall bladder with thick walls, containing turbid, thick-flowing liquid and plenty of stones. The temperature after the operation around 39°C. Died 5 days after the operation.

No autopsy.

It is possible that the morbid process in the gall bladder in this case might have improved under conservative treatment, as the temperature was decreasing the day after admittance.

In 5 cases the cholecystitis was complicated by circumscribed or widespread, purulent peritonitis.

19) A 744/1924. Man, aged 47. Several attacks over 1 year. Latest attack the day before admittance.

Admitted on Sep. 23. Strongly affected, cyanotic, fat. Temp. 38,6°C. Large, distended, very taut abdomen with marked rigidity in the upper right portion. After a strong stimulation *cholecystostomy*. Local anesthesia, narcosis. In the abdomen about 1 liter of thin, faintly blood-coloured liquid. Heavily distended gall bladder whose gangrenous fundus was cut off; it contained a plum-sized stone. Tamponade. Sep. 25. Died.

Autopsy: acute gangrenous cholecystitis; fatty liver.

20) 1925/1930. Woman, aged 62. 3 attacks of gall stones for 3 weeks. Latest attack the day before admittance.

Admitted on July 7. Affected general condition. Jaundiced. Temp. 37,7°C. Slight tenderness over the region of the gall bladder. July 9. The temp. which on July 8 was 38,6°C, increased to 40°C with chills. Intense tenderness in the whole right portion of the abdomen. The same day *cholecystectomy*. Wholly gangrenous gall bladder, surrounded by bile-coloured exudate and containing liquid stinking of coli. In the gall bladder several stones. Died the day after the operation with signs of cardiac insufficiency.

Autopsy: fatty heart and liver; postoperative peritonitis. The peritonitis was peripheral and superficial.

When the temperature rose from 37,7°C to 38,6°C the day after admittance, the patient should perhaps have been operated on that day, and, since she was both fairly old and strongly affected generally, only *cholecystostomy* ought maybe to have been performed.



21) 2359/1930. Man, aged 42. First attack of gall stone disease which set in the day before admittance. Mentally diseased.

Admitted on Aug. 21. Affected condition. Temp. 37,9°C. Tenderness and rigidity in the upper right portion of the abdomen. Aug. 22. *Cholecystectomy*. Avertin narcosis. The gall bladder covered by the omentum; when this was loosened, stinking pus welled up. Large perforation in the fundus of the gall bladder. Abundance of stones in the gall bladder. Aug. 23. Died.

No autopsy.

22) 2506/1930. Man, aged 50. First attack, setting in 2 days prior to admittance.

Admitted on Sep. 6. Affected general condition. Temp. 38,7°C. In the urine plenty of albumin. Distended and taut abdomen. Marked tenderness and rigidity in the right upper portion of the abdomen. The same day *cholecystectomy*. In the peritoneum plenty of thin pus. The gall bladder distended, covered by fibrin, containing stinking pus; the mucous membrane gangrenous. 12 stones. Sep. 11. The quantity of urine decreased to 150 c. c. during the last 24 hours. Mentally dulled. Blood pressure 100/50. Sep. 13. Died from uremia.

Autopsy: circumscribed peritonitis; amyloidosis of the kidneys. The liver brittle, grey like clay, containing fat. (Microscopical examination: lipomatous degeneration.) Kidneys: (micr.) amyloid nephrocirrhosis.

23) 763/1934. Woman, aged 62. First attack, setting in 4 days prior to admittance.

Admitted on Feb. 27. Affected general condition. Temp. 39,1°C. Dyspneic. Intense tenderness and rigidity in the right upper portion of the abdomen down to the plane of the navel. As the patient was fairly weak and the local symptoms not too alarming, an expectant treatment was decided on. — During the following days the patient improved, the temp. decreased to 37,5°C, but the pulse kept around 120. On March 2 the quantity of urine decreased to 80 cc. in 24 hours, and the rest nitrogen in the blood was 138. An acute change for the worse with pronounced symptoms of peritonitis in the whole right portion of the abdomen. The same day *cholecystostomy* under local anesthesia and mild narcosis. In the abdomen an abundance of dirty grey liquid containing rods. The lower surface of the gall bladder was perforated approximately midway between the fundus and the collum. It contained a number of stones. Died the same day.

Autopsy: bilious peritonitis; gangrenous perforative cholecystitis; cholelithiasis; hypertrophy and dilatation of the heart; lipomatous infiltration of the heart and the pancreas; parenchymatous degeneration of the liver.

The patient was strongly affected generally at the admittance to the hospital, but as the local symptoms were not too alarming, an expectant treatment was tried the next few days. An acute change for the worse, however, set in after 3 days, probably on account of perforation of the gangrenous gall bladder; the operation now performed could not save the patient. In addition to this, the patient

showed symptoms of grave disturbance of the liver function with obliguria and marked increase of rest nitrogen in the blood. The fact that the pulse remained high the first days in spite of the decrease in temperature, should have served as an indication that the morbid process was more serious than the other clinical symptoms seemed to imply. The patient ought to have been operated on earlier, but even so it is not very probable that she could have been saved by an operation.

In 4 cases the cholecystitis was complicated by acute pancreatitis.

24) 1748/1928. Woman, aged 67. In 1922 treated for her first attack of gall stone disease. Since that time recurrent attacks.

Admitted on June 30 after the latest attack. The general condition affected, temp. 37,5°C. Marked tenderness and rigidity over the region of the gall bladder. July 2. After a temporary improvement again a change for the worse with pronounced peritoneal irritation. Temp. 38,9°C. Pulse 106. On vital indication *cholecystectomy* was performed. Local anesthesia, mild ether narcosis. Round the gall bladder a circumscribed accumulation of bile. The gall bladder entirely gangrenous, containing white bile mixed with pus. The pancreas was much thickened and hard, particularly at the caput, where fatty necroses were found. A catheter was introduced through the stump of the cystic duct into the common bile duct. June 12. Begins to be out of bed. July 19. After temporary improvement again worse. Frequent vomitings. July 20. X-ray examination: heavy distension of the stomach and the duodenum as far as the site of crossing at the mesenterial root. »No doubt exacerbation of the pancreatitis.» July 28. Increasingly worse with repeated vomitings. The condition too poor to allow of operation. Died.

No section.

25) B 657/1924. Woman, aged 60. 3 attacks for 7 years. Latest attack 2 days prior to admittance.

Admitted on Sep. 18. General condition comparatively good. Temp. 38,6°C. The abdomen heavily distended, diffusely tender, rigidity particularly over the navel. Sep. 22. Rising temperature, resistance over the region of the gall bladder. *Cholecystectomy*. Local anesthesia and narcosis. Turbid, greyish yellow liquid in the right subphrenic room. The gall bladder walled in by adhesions. It contained purulent liquid; the wall interspersed with abscesses; 4 stones. Died a few hours after the operation.

Autopsy: circumscribed fibrinous peritonitis; acute pancreatitis; fatty necroses of the omentum; myocarditis; cardiosclerosis.

26) 2173/1929. Woman, aged 62. First attack which set in 18 hours prior to admittance.

Admitted on Aug. 29. Affected general condition. Temp. 38,3°C. Tenderness and rigidity in the right upper portion of the abdomen. Aug. 30.

The temp. has decreased to 38°C. *Cholecystectomy*. Narcosis. Inflamed gall bladder, the size of a goose-egg, with numerous stones. Sep. 2. Rising temp. Diastase value in the urine 256. Sep. 5. Died, increase of temp. up to 41,8°C.

Autopsy: purulent bronchitis; numerous fatty necroses round the pancreas. In the latter a nut-sized abscess with turbid contents.

27) 2756/1929. Woman, aged 61. 2 attacks over a period of  $\frac{3}{4}$  year. Latest attack one week prior to admittance.

Admitted on Nov. 3. Good general condition. Mild jaundice. Temp. 37,8°C. Rigidity and tenderness over the region of the gall bladder. Nov. 6. Temp. as before. Deteriorated general condition, increased jaundice. *Cholecystectomy*. Narcosis. Distended gall bladder, containing turbid liquid. The wall showed inflammatory changes. The mucous membrane ulcerated. One stone. Nov. 8. Died from sepsis.

Autopsy: acute pancreatitis. Heavily swollen pancreas, containing numerous fatty necroses.

The survey of the deaths after operation for acute cholecystitis, which we have given above, comprises all the cases operated on for acute cholecystitis in the years 1922—1935, irrespectively of the method of operation employed. In 248 cases, cholecystectomy was performed, and in 9 cases cholecystostomy was made. The cases in which only cholecystostomy could be performed, are as a rule by far the most severe cases. On account of this, the mortality for these cases is considerably higher than for the cases of cholecystectomy. The selection of the cases in which cholecystostomy is performed and of the cases in which cholecystectomy is made, is different in different hospitals; this might in its turn result in a different mortality in the materials. If we want to obtain an idea of the risk involved in operation for a certain complaint, we must include in the material all the cases operated on, irrespectively of the kind of operation performed. The same is true if we want to compare a material of cases operated on with another such material.

During the years 1922—1935, the total number of cases operated on for acute cholecystitis was 257. Of these 27 died, i. e. 10,5 per cent of the operations. During the latter years of the period in which the material was collected, the postoperative mortality was lower than in the preceding years. If the material is divided into three groups: the first group comprising the cases which were operated on during the years 1922—1927, the second those operated on during the years 1928—1931, and the third those operated on in the years 1932—1935 (see table 26), and if the mortality is calculated for the groups, we find that in the first two groups it





is about equally high (14,8 and 13,3 per cent respectively); in the third group, on the other hand, it is considerably lower (3,5 per cent). The difference in mortality between the first two groups taken together, and the last group, is statistically significant (diff. =  $10,6 \pm 3,3$ ). In the material are included 20 cases which had previously been treated for acute cholecystitis and not operated on on that occasion. Out of these, one died. If regard is only paid to the cases which were operated on during the first stay in hospital, the figures of mortality are 15,7, 13,3, and 3,8 per cent. The difference in mortality between the first two groups, taken together, and the last group is statistically significant (diff. =  $10,8 \pm 3,6$ ).

A change in the mortality of a material of cases operated on may be due to a number of different factors. When we are concerned with a disease, like the one under discussion, in which only part of the cases are treated operatively, we must pay regard to the fact that the cases operated on make up a selection of the material. This selection may be made in various ways, which in its turn may cause changes in the postoperative mortality. If we are to obtain an idea of the factors which are liable to affect the mortality, we must analyse the total material of acute cholecystitis as well as the part of the material which was operated on and the part which was not subjected to an operation.

The material of cases of cholecystitis has shown an almost annual increase. During the years 1922—1927, an average number of 28,5 patients were annually admitted to the hospital, during the years 1928—1931, 41,3, and in the years 1932—1935, 52,5 patients. This increase in the material makes itself felt chiefly among the patients not operated on, whereas the annual number of patients operated on has shown an increase, it is true, but a smaller one (see table 27). As the increase in the material has chiefly taken place among the patients not operated on, the relation between cases not operated on and cases operated on has changed. In the years 1922—1927, 48,5 per cent of the cases of cholecystitis were operated on, during their first stay in the hospital in the years 1928—1931, 45,5 per cent, and in the years 1932—1935, 37,6 per cent. It is thus principally in the years when the postoperative mortality was lower, that a comparatively smaller part of the cases of acute cholecystitis were operated on.

Table 27. *Means for the annual number of cases of acute cholecystitis treated for the first time.*

| Group                 | Period    | Means of annually treated cases |       |       |
|-----------------------|-----------|---------------------------------|-------|-------|
|                       |           | Men                             | Women | Total |
| Not operated.....     | 1922—1927 | 3,5                             | 11,2  | 14,7  |
| »       »       ..... | 1928—1931 | 7,5                             | 15,0  | 22,5  |
| »       »       ..... | 1932—1935 | 9,3                             | 23,5  | 32,8  |
| Operated.....         | 1922—1927 | 2,3                             | 11,5  | 13,8  |
| »       .....         | 1928—1931 | 3,0                             | 15,8  | 18,8  |
| »       .....         | 1932—1935 | 2,3                             | 17,5  | 19,8  |
| Total .....           | 1922—1927 | 5,8                             | 22,7  | 28,5  |
| »       .....         | 1928—1931 | 10,5                            | 30,8  | 41,3  |
| »       .....         | 1932—1935 | 11,5                            | 41,0  | 52,5  |

Theoretically speaking it is naturally conceivable that when the material increases, this may mean that a larger number of mild cases are included. If the same percentage of cases as before is then operated on, this also brings about a displacement in the group of operations to the effect that it will include a larger number of mild cases. If, however, a decrease in the percentage of cases operated on takes place so that a smaller part is operated on when the material increases, we have rather reason to suspect that the indications for operation have remained constant. These are theoretical arguments. We may naturally conceive of displacements in other directions, e. g. that the material increases without the percentage of mild cases increasing, and so on. We cannot arrive at definite conclusions except by a direct examination.

In the first place we shall examine the total material of acute cholecystitis in regard to the changes through which the material has possibly passed during the abovementioned periods, and try to obtain an idea as to whether the selection of the patients operated on has been made according to similar, or different, principles. For this purpose we have to treat the material with regard to the patients' first stay in the hospital. The cases which were operated on during a subsequent stay in the hospital, are here treated as cases not operated on.

In table 28 the material is divided according to the age of the patients. The table shows that no obvious change has taken place in the age distribution.

Table 28. *All cases of acute cholecystitis. Distribution according to age, at first stay in hospital, of cases not-operated on and cases operated on. The periods 1922—1931 and 1932—1935.*

| Age,<br>years | 1922—1931          |                 |                    |             |                    |                     | 1932—1935          |                 |                    |             |                    |             |
|---------------|--------------------|-----------------|--------------------|-------------|--------------------|---------------------|--------------------|-----------------|--------------------|-------------|--------------------|-------------|
|               | Not operated       |                 | Operated           |             | Not op. + op.      |                     | Not operated       |                 | Operated           |             | Not op.            |             |
|               | Number<br>of cases | % of<br>not op. | Number<br>of cases | % of<br>op. | Number<br>of cases | % of not<br>op.+op. | Number<br>of cases | % of<br>not op. | Number<br>of cases | % of<br>op. | Number<br>of cases | % of<br>op. |
| Under 20      | 2                  | 1,1             | —                  | —           | 2                  | 0,6                 | 1                  | 0,8             | —                  | —           | 1                  | —           |
| 20—29         | 10                 | 5,6             | 11                 | 7,0         | 21                 | 6,2                 | 3                  | 2,3             | 4                  | 5,1         | 7                  | —           |
| 30—39         | 16                 | 9,0             | 31                 | 19,6        | 47                 | 14,0                | 9                  | 6,9             | 23                 | 29,1        | 32                 | —           |
| 40—49         | 26                 | 14,6            | 43                 | 27,2        | 69                 | 20,5                | 14                 | 10,7            | 15                 | 19,0        | 29                 | —           |
| 50—59         | 41                 | 23,0            | 37                 | 23,4        | 78                 | 23,2                | 30                 | 22,9            | 22                 | 27,8        | 52                 | —           |
| 60—69         | 50                 | 28,2            | 29                 | 18,4        | 79                 | 23,6                | 45                 | 34,3            | 12                 | 15,2        | 57                 | —           |
| 70—79         | 28                 | 15,7            | 7                  | 4,4         | 35                 | 10,4                | 22                 | 16,8            | 3                  | 3,8         | 25                 | —           |
| 80—89         | 5                  | 2,8             | —                  | —           | 5                  | 1,5                 | 7                  | 5,3             | —                  | —           | 7                  | —           |
| Total         | 178                | 100,0           | 158                | 100,0       | 336                | 100,0               | 131                | 100,0           | 79                 | 100,0       | 210                | 100,0       |

The material might have changed not only as regards the age of the patients but also as regards the more or less severe grade of the disease. In order to get an idea of the extent to which such a change has possibly occurred, we divided the cases into three groups.

I. *Mild cases.* Increase of temperature up to 38°C, tenderness, and possibly resistance, at the site of the gall bladder, no, or slight, peritoneal irritation. The clinical symptoms of infection in the gall bladder were in these cases modest.

II. *Medium-severe cases.* The temperature kept between 38° and 39°C. The patient presented marked symptoms of cholecystitis in the form of tenderness, possibly a palpable resistance, and more or less pronounced rigidity over the region of the gall bladder. The disease did not, however, to a high degree affect the general state of health, and the cases were of a type which was not as a rule considered to indicate an immediate operation.

III. *The severe cases.* The patient was frequently taken ill with shaking chills. The general state of health was affected. The temperature kept between 39° and 40°C, the pulse was affected. A marked peritoneal irritation was present round the site of the gall bladder, and frequently in the whole upper portion of the abdomen, in exceptional cases over the whole of the abdomen.

Table 29. *All cases of acute cholecystitis. Distribution of cases operated on and cases not operated on according to grade of disease. The years 1922—1931 and 1932—1935.*

| Grade of disease    |                | 1922—1931    |          |                    | 1932—1935    |          |                    |
|---------------------|----------------|--------------|----------|--------------------|--------------|----------|--------------------|
|                     |                | Not operated | Operated | Not op. + operated | Not operated | Operated | Not op. + operated |
| Mild cases          | No. of cases   | 43           | 21       | 64                 | 40           | 13       | 53                 |
|                     | % of all cases | 24,2         | 13,5     | 19,2               | 30,5         | 16,0     | 25,0               |
| Medium severe cases | No. of cases   | 101          | 89       | 190                | 61           | 39       | 100                |
|                     | % of all cases | 56,7         | 57,0     | 56,8               | 46,6         | 48,2     | 47,2               |
| Severe cases        | No. of cases   | 34           | 46       | 80                 | 30           | 29       | 59                 |
|                     | % of all cases | 19,1         | 29,5     | 24,0               | 22,9         | 35,8     | 27,8               |
| All cases           | No. of cases   | 178          | 156      | 334                | 131          | 81       | 212                |
|                     | % of all cases | 100,0        | 100,0    | 100,0              | 100,0        | 100,0    | 100,0              |

A grouping of the material according to the more or less severe grade of the disease naturally must be fairly rough. The division might however be of a certain value, if we want to get an idea of the general composition of the material and to find out whether the latter has been subject to any considerable changes.

In table 29 the material is divided into these three groups. It shows that no marked change has occurred in the material. Both the mild and the severe cases show some relative increase in the latter years.

The total material of acute cholecystitis consequently presented no marked changes in regard to the age of the patients and the grade of the disease. We shall further examine the cases not operated on.

In table 28, the cases not operated on are arranged according to the age at the time of the first stay in hospital. During the years 1932—1935, the older patients occur in a somewhat greater percentage than previously. The difference, however, is comparatively unimportant. In table 29 the cases are arranged according to the grade of the disease. During the years 1932—1935, the relative number of mild and severe cases increased. The changes found in the composition of the material with regard to the more or less severe grade of disease of the cases, are not particularly pronounced,



however. As, further, the grouping of the material according to the grade of the disease is fairly rough, we may only, on the basis of these data, observe that no marked changes are present.

The mortality of the cases not operated on was 6,8 per cent for the years 1922—1927, 6,7 per cent for the years 1928—1931, and 6,1 per cent for the years 1932—1935. We have above (p. 77), relative to the discussion of the cases not operated on, pointed out that it is not probable that, by an operative interference, any one of those who died, might have been saved. The fairly similar percentage mortality of the cases of acute cholecystitis not operated on, consequently, in spite of the fact that the material has increased, cannot indicate that the advanced cases were operated on to a smaller extent than previously.

In the material of cases operated on for acute cholecystitis, we did not include the cases presenting stone in the common bile duct (see p. 102). We may count with the fact that a number of cases with stone in the common bile duct are found among the patients not operated on. In the 19 cases not operated on in which a post-mortem examination was performed, stone in the common bile duct was found in no less than 7 cases. It is not probable that stone in the common bile duct has been present to an equal extent in the remaining material. Among the total number of cases operated on (620), stone in the common bile duct was found in 102 cases (16,5 per cent). This frequency of stone in the common bile duct tallies well with the one found by other writers (LIEDBERG about 17 per cent among cases of cholecystitis; WILKIE 18 per cent, CLUTE 17,9 per cent, and LAHEY 21,2 per cent among cases operated on for gall stone disease; CRUMP 24 per cent of cases of gall stone in autopsy material). It is to be supposed that the frequency of stone in the common bile duct among the cases not operated on is not higher than among the cases operated on, as the majority of cases presenting common duct stone are no doubt operated on. It might consequently be justified to calculate the mortality among the cases of cholecystitis not operated on, after removal of the 7 cases in which stone in the common bile duct was found in the post-mortem examination. We find that the mortality is 5,7 per cent for the years 1922—1931 and 2,4 per cent for the years 1932—1935. The difference in mortality is statistically not probable (diff. =  $3,3 \pm 2,4$ ).

We have consequently reason to assert that neither the total material of acute cholecystitis, nor the cases not operated on, have shown any obvious changes. The small changes in the material which have been demonstrated cannot explain the decreased post-operative mortality during the years 1932—1935. It now remains to examine the cases operated on.

In table 28 the cases operated on are grouped with regard to the age at the admittance to the hospital, and in table 29 according to the more or less severe grade of the disease. The material shows no marked change with regard to the age distribution. In the years 1932—1935, however, a comparatively larger number of severe cases were operated on than in the previous years. The difference is not statistically significant, however, or even probable (diff. =  $3,8 \pm 4,71$ ). The mild cases also showed some relative increase. In spite of the fact that the grouping of the material, according to the grade of the disease, is fairly rough, it shows that the relative number of severe cases at least was not smaller than in the preceding years.

The material of cases operated on thus shows no obvious change in regard to the age distribution or the grade of the disease during the different periods of years (if, in the material of cases operated on, we include the 20 cases which had been treated in the hospital on a previous occasion without then being operated on, the above-mentioned changes in the material of operations remain the same, that is to say fairly unimportant.)

We consequently cannot explain the decreased postoperative mortality during the years 1932—1935 by the available material of cholecystitis having changed or by a selection being made among the patients operated on to the effect that milder cases or younger patients were operated on to a larger extent than formerly. A selection, on the other hand, has naturally taken place in that a smaller portion of the material was operated on than previously (see p. 142). This selection, however, cannot very well influence the mortality.

In the first place we should then consider the changes which may have taken place in the technique of operation and in the treatment of the patients prior to, or after, the operation. During the years 1922—1931, most of the patients were operated on under general narcosis, and only a small number under local anesthesia; in the years 1932—1935, on the other hand, local, and particularly spinal,

anesthesia began to be used to a larger extent. It is, however, only from the year 1935 that spinal anesthesia came to be used in the majority of operations for gall stone disease. It is remarkable that all the 7 post-operative deaths from pulmonary disease occurred during the years 1922—1931. The change in the method of anesthesia which was carried through in the latter period, may have lessened the risk of postoperative pneumonia. It should be stated however, that it cannot be considered as established that spinal anesthesia brings with it a smaller death-risk than ether narcosis (at least in the case of patients who do not present changes of the lungs, injuries to the liver, etc.). BOYCE, VEAL and Mc FETRIDGE, for instance, in their material of cases operated on for acute cholecystitis, found no difference in mortality among the cases in which spinal anesthesia had been adopted as compared to those subjected to ether narcosis. R. KALJSER, in a material comprising 142 operations for gall stone disease, performed under narcosis, and 545 operations performed under spinal anesthesia, was not able to find a statistically significant, or probable, difference in mortality between the cases operated on under narcosis, and those operated on under spinal anesthesia. In regard to the treatment of the patients before and after the operation, attention has been more and more paid in recent years to the liquid balance and liver function of the patient. Plenty of liquid and plenty of food substances rich in carbohydrates are being administered, in many cases glycosis subcutaneously or intravenously, sometimes with insulin, both before and after the operation. It is obvious that this may be of a certain importance to the reduced mortality, as we know that the liver in acute cholecystitis may be more or less injured and in the severe cases certainly is injured.

We have further to examine whether the indications for operation have changed. In the following discussion we shall treat all the cases operated on for acute cholecystitis, that is also the 20 cases which were not operated on during the first stay in hospital but only at a subsequent stay. The first point to investigate is whether the patients during the different periods were operated on in the same stage of the disease, or whether any change has taken place in this respect. In table 30 all the cases operated on for acute cholecystitis are divided according to the time which has elapsed between the beginning of the attack and the operation (in 15 cases data

Table 30. *All cases of acute cholecystitis operated on. Cumulative distribution according to length of interval between beginning of attack and operation within different periods of time.*

| Interval between beginning of attack and operation | 1922—1927       |                       | 1928—1931       |                       | 1922—1931       |                       | 1932—1935       |                       | Difference between percentage figures for the years 1922—31 and 1932—35 |
|----------------------------------------------------|-----------------|-----------------------|-----------------|-----------------------|-----------------|-----------------------|-----------------|-----------------------|-------------------------------------------------------------------------|
|                                                    | Number of cases | % of total year group | Number of cases | % of total year group | Number of cases | % of total year group | Number of cases | % of total year group |                                                                         |
| 0—1 day .....                                      | 6               | 7,4                   | 4               | 5,1                   | 10              | 6,3                   | 3               | 3,7                   | +2,6 ± 2,8                                                              |
| 0—2 days.....                                      | 15              | 18,5                  | 14              | 17,7                  | 29              | 18,1                  | 10              | 12,2                  | +5,9 ± 4,1                                                              |
| 0—3 » .....                                        | 21              | 25,9                  | 25              | 31,6                  | 46              | 28,8                  | 10              | 12,2                  | +16,6 ± 5,1                                                             |
| 0—4 » .....                                        | 28              | 34,6                  | 33              | 41,8                  | 61              | 38,1                  | 13              | 15,9                  | +22,2 ± 5,6                                                             |
| 0—5 » .....                                        | 34              | 42,0                  | 38              | 48,1                  | 72              | 45,0                  | 14              | 17,1                  | +27,9 ± 5,7                                                             |
| 0—6 » .....                                        | 46              | 56,8                  | 46              | 58,2                  | 92              | 57,5                  | 23              | 28,0                  | +29,5 ± 6,3                                                             |
| Within 1 week                                      | 56              | 69,1                  | 51              | 64,6                  | 107             | 66,9                  | 31              | 37,8                  | +29,1 ± 6,5                                                             |
| » 3 weeks                                          | 81              | 100,0                 | 78              | 98,7                  | 159             | 99,4                  | 79              | 96,3                  | +3,1 ± 2,2                                                              |
| Total                                              | 81              | 100,0                 | 79              | 100,0                 | 160             | 100,0                 | 82              | 100,0                 | —                                                                       |

are lacking on the interval between the onset of the attack and the admittance to the hospital; these cases are not included in the table). The table shows that in the years 1922—1927, as in the years 1928—1931, fifty per cent of the cases were operated on within six days of the beginning of the attack, while in the years 1932—1935, fifty per cent of the cases were operated on only when more than a week had passed after the beginning of the attack (on the 9th day). In the table, the percentage is calculated for the cases which were operated on within 24 hours after the beginning of the attack, within 48 hours, and so on. Differences are calculated for the percentages of cases operated on in the years 1922—1931 and 1932—1935. We find that no statistically significant difference is present between the different periods of time for the percentage number of cases operated on within 24, or within 48, hours. A statistically significant difference, on the other hand, is present for the percentage number of cases operated on within 3 days in the former period as compared to the years 1932—1935. The difference is statistically significant also for the cases which were operated on within four days, five days, and so on. In other words, a displacement has taken place in the time at which the operation was performed: *during the years 1932—1935, the patients were operated on in a later stage of the disease.* The fact that this displacement in the time at which the operation was made,



for the cases operated on from the third day after the beginning of the attack onwards, is statistically significant, shows that it is not determined by chance. As pointed out above, it was avoided in the clinic, if possible, to operate on the patients during the most acute stage. In earlier years, as seen in the tables, a comparatively large number of cases were operated on during an early stage of the disease. In the course of time, physicians have become more and more convinced that in the majority of cases, they may without risk wait for the remission of the acute symptoms and operate only in a later stage of the disease.

Table 31. *Cases of acute cholecystitis, operated on in 1922—1927, 1928—1931 and 1932—1935. Cumulative distribution according to length of interval between beginning of attack and admittance to hospital.*

| Interval between<br>beginning of attack<br>and admittance | 1922—1927          |                          | 1928—1931          |                          | 1932—1935          |                          |
|-----------------------------------------------------------|--------------------|--------------------------|--------------------|--------------------------|--------------------|--------------------------|
|                                                           | Number<br>of cases | % of total<br>year group | Number<br>of cases | % of total<br>year group | Number<br>of cases | % of total<br>year group |
| 0—1 day .....                                             | 28                 | 34,6                     | 38                 | 48,1                     | 42                 | 51,2                     |
| 0—2 days .....                                            | 47                 | 58,0                     | 51                 | 64,6                     | 58                 | 70,7                     |
| 0—3 » .....                                               | 60                 | 74,1                     | 57                 | 72,2                     | 62                 | 75,6                     |
| 0—4 » .....                                               | 70                 | 86,4                     | 63                 | 79,7                     | 70                 | 85,4                     |
| 0—5 » .....                                               | 71                 | 87,7                     | 69                 | 87,3                     | 77                 | 93,9                     |
| 0—6 » .....                                               | 74                 | 91,4                     | 71                 | 89,9                     | 79                 | 96,3                     |
| 0—7 » .....                                               | 76                 | 93,8                     | 75                 | 94,9                     | 80                 | 97,6                     |
| Within 3 weeks                                            | 81                 | 100,0                    | 79                 | 100,0                    | 82                 | 100,0                    |
| Total                                                     | 81                 | 100,0                    | 79                 | 100,0                    | 82                 | 100,0                    |

It might be objected that this displacement in time of the operation may be due to the fact that the patients have in recent years been admitted to the hospital in a later stage of their disease than previously. As, however, the patients who do not live in the city of Uppsala, by improved communications must find it easier to come to the hospital and as, further, an ever increasing number of the persons suffering from gall stone disease have come to the hospital for treatment in recent years, we should rather expect the patients to have come to the hospital in an earlier stage of the disease in recent years. As is seen in table 31, 34,6 per cent of the patients had been admitted to the hospital during the first 24 hours of the onset of the attack in the years 1922—1927, 48,1 per cent in the

years 1928—1931, and 51,2 per cent in the years 1932—1935. The percentage figures given show that the patients in recent years have been admitted to the hospital in a somewhat earlier stage of the disease and that, consequently, if the patients had been operated on in the same stage of the disease as formerly, we should expect to find in the latter period a larger number of patients operated on in an early stage of the disease instead of the other way round.

If we examine the interval between the patients' admittance to the hospital and the operation (table 32), we find that in the years 1922—1931, fifty per cent of the patients had been operated on

Table 32. *Cases of acute cholecystitis, operated on in 1922—1931 and 1932—1935. Cumulative distribution according to length of interval between admittance to hospital and operation.*

| Interval between admittance and operation | 1922—1931       |                       | 1932—1935       |                       | Difference between the percentage figures for the two year groups |
|-------------------------------------------|-----------------|-----------------------|-----------------|-----------------------|-------------------------------------------------------------------|
|                                           | Number of cases | % of total year group | Number of cases | % of total year group |                                                                   |
| 0—1 day .....                             | 39              | 22,8                  | 10              | 11,6                  | +11,2 $\pm$ 4,7                                                   |
| 0—2 days.....                             | 66              | 38,6                  | 13              | 15,1                  | +23,5 $\pm$ 5,4                                                   |
| 0—3 » .....                               | 89              | 52,0                  | 18              | 20,9                  | +31,1 $\pm$ 5,8                                                   |
| 0—4 » .....                               | 109             | 63,7                  | 24              | 27,9                  | +35,8 $\pm$ 6,1                                                   |
| 0—5 » .....                               | 126             | 73,7                  | 31              | 36,0                  | +37,7 $\pm$ 6,2                                                   |
| 0—6 » .....                               | 142             | 83,0                  | 41              | 47,7                  | +35,3 $\pm$ 6,1                                                   |
| 0—7 » .....                               | 149             | 87,1                  | 48              | 55,8                  | +31,3 $\pm$ 5,9                                                   |
| Within 3 weeks                            | 170             | 99,4                  | 85              | 98,8                  | +0,6 $\pm$ 1,3                                                    |
| Total                                     | 171             | 100,0                 | 86              | 100,0                 | — —                                                               |

within three days of the admittance. In the years 1932—1935, on the other hand, fifty per cent of the patients had been operated on only within 7 days of the admittance to the hospital. The table shows the percentage number of cases which were operated on within 24 hours of the admittance to the hospital, within 48 hours, and so on, for the years 1922—1931 and 1932—1935. No statistically probable difference is present for the percentage number of those who in the former or the latter period were operated on within the first 24 hours of the admittance to the hospital. On the other hand, there is a *statistically significant difference between the two periods for those who were operated on within two days, within three days, etc., of the admittance to the hospital.*

Table 33. All cases of acute cholecystitis operated on. Cumulative distribution according to length of interval between admittance to hospital and operation combined with length of interval between beginning of attack and admittance to hospital. The periods 1922—1931 and 1932—1935.

| Interval between admittance and operation |                 | 1922 — 1931                                         |                 |                     |                 |                     |                 |                     |                 |                     |                 | 1932 — 1935         |                 |                     |                 |                     |                 |                     |                 |                     |    |
|-------------------------------------------|-----------------|-----------------------------------------------------|-----------------|---------------------|-----------------|---------------------|-----------------|---------------------|-----------------|---------------------|-----------------|---------------------|-----------------|---------------------|-----------------|---------------------|-----------------|---------------------|-----------------|---------------------|----|
|                                           |                 | Interval between beginning of attack and admittance |                 |                     |                 |                     |                 |                     |                 |                     |                 |                     |                 |                     |                 |                     |                 |                     |                 |                     |    |
|                                           |                 | 1 day                                               | 2 days          | 3-7 days            | > 7 days        | Unknown             | All days        | 1 day               | 2 days          | 3-7 days            | > 7 days        | Unknown             | All days        | 1 day               | 2 days          | 3-7 days            | > 7 days        | Unknown             | All days        |                     |    |
|                                           | Number of cases | oper. in % of total                                 | Number of cases | oper. in % of total | Number of cases | oper. in % of total | Number of cases | oper. in % of total | Number of cases | oper. in % of total | Number of cases | oper. in % of total | Number of cases | oper. in % of total | Number of cases | oper. in % of total | Number of cases | oper. in % of total | Number of cases | oper. in % of total |    |
| Within 1 day .....                        | 18              | 27                                                  | 8               | 25                  | 12              | 23                  | -               | -                   | 1               | 9                   | 39              | 23                  | 6               | 14                  | 2               | 13                  | 9               | -                   | -               | 10                  | 12 |
| » 2 days.....                             | 33              | 50                                                  | 11              | 34                  | 20              | 38                  | 1               | 11                  | 1               | 9                   | 66              | 39                  | 7               | 17                  | 3               | 19                  | 3               | 14                  | -               | 13                  | 15 |
| » 3 » .....                               | 42              | 64                                                  | 14              | 44                  | 27              | 51                  | 2               | 22                  | 4               | 36                  | 89              | 52                  | 9               | 21                  | 3               | 19                  | 5               | 23                  | 1               | 25                  | 18 |
| » 4 » .....                               | 46              | 70                                                  | 19              | 59                  | 34              | 64                  | 6               | 67                  | 4               | 36                  | 109             | 64                  | 10              | 24                  | 4               | 25                  | 9               | 41                  | -               | 1                   | 25 |
| » 5 » .....                               | 54              | 82                                                  | 22              | 69                  | 37              | 70                  | 8               | 89                  | 5               | 45                  | 126             | 74                  | 14              | 33                  | 6               | 38                  | 9               | 41                  | 1               | 50                  | 21 |
| » 6 » .....                               | 57              | 86                                                  | 26              | 81                  | 44              | 83                  | 9               | 100                 | 6               | 55                  | 142             | 83                  | 20              | 48                  | 8               | 50                  | 11              | 50                  | 1               | 50                  | 31 |
| » 7 » .....                               | 61              | 92                                                  | 27              | 84                  | 44              | 83                  | 9               | 100                 | 8               | 73                  | 149             | 87                  | 24              | 57                  | 10              | 63                  | 12              | 55                  | 1               | 50                  | 48 |
| Total                                     | 66              | 100                                                 | 32              | 100                 | 53              | 100                 | 9               | 100                 | 11              | 100                 | 171             | 100                 | 42              | 100                 | 16              | 100                 | 22              | 100                 | 4               | 100                 | 86 |

Consequently, a *significant displacement has occurred in the time which elapsed both between the beginning of the attack and the operation, and between the admittance to the hospital and the operation in that the patients during the years 1932—1935 were operated on in a later stage of the disease, or when a longer time had elapsed after they had been admitted to the hospital.*

This may also be illustrated in another way. In table 33, the material is grouped both according to the interval between the beginning of the attack and the admittance to the hospital, and also according to the interval between the admittance to the hospital and the operation. In the years 1922—1931, fifty per cent of the cases which were admitted during the first 24 hours of the disease, were operated on within two days of the admittance to the hospital. In the years 1932—1935, on the other hand, fifty per cent of the patients which were admitted to the hospital during the first 24 hours of the disease, were operated on only within 6—7 days of the admittance to the hospital. In the table may be read the corresponding figures for the patients who were admitted during the second day of the disease, and during the third up to the seventh day of the disease. The patients who were admitted to the hospital during the first 24 hours of the disease, are the most severe cases. The mortality among those is also comparatively high. In the years 1922—1931, 12 died out of the 66 who were admitted during the first 24 hours of the disease, and in the years 1932—1935, 2 died out of 42 (see table 34). Fifty per cent of the deaths after operation for acute cholecystitis in our material occurred among the patients which were admitted during the first 24 hours of the disease. Of the remaining 12 deaths during the years 1922—1931, 6 were admitted during the second day of the disease; of the others, 5 were admitted to the hospital during the 3rd—7th day of the disease; one patient, finally, was only admitted 11 days after the beginning of the attack. The second patient who died in the years 1932—1935 was admitted to the hospital 4 days after the onset of the attack.

The majority of the deaths in the material thus occurred among the patients who were admitted to the hospital in an early stage of the disease, i. e. among the most severe cases. If we calculate the mortality among those who were admitted to the hospital during the first two days of the disease, we find that, for the years 1922—



Table 34. *All cases of acute cholecystitis operated on, and deaths. Distribution according to length of interval between admittance to hospital and operation, combined with interval between beginning of attack and admittance to hospital. The years 1922—1931 and 1932—1935.*

| Interval between<br>admittance and<br>operation |                       | 1922—1931                                           |                       |                    |                       |                    |                       |                    |                       |                    |                       | 1932 1935          |                       |                    |                       |                    |                       |                    |                       |                    |                       |                    |                       |
|-------------------------------------------------|-----------------------|-----------------------------------------------------|-----------------------|--------------------|-----------------------|--------------------|-----------------------|--------------------|-----------------------|--------------------|-----------------------|--------------------|-----------------------|--------------------|-----------------------|--------------------|-----------------------|--------------------|-----------------------|--------------------|-----------------------|--------------------|-----------------------|
|                                                 |                       | Interval between beginning of attack and admittance |                       |                    |                       |                    |                       |                    |                       |                    |                       |                    |                       |                    |                       |                    |                       |                    |                       |                    |                       |                    |                       |
| 0—1 day                                         |                       | 2 days                                              |                       | 3—7 days           |                       | > 7 days           |                       | Unknown            |                       | All days           |                       | 0 1 day            |                       | 2 days             |                       | 3—7 days           |                       | > 7 days           |                       | Unknown            |                       | All days           |                       |
| Number<br>of cases                              | deaths<br>among these | Number<br>of cases                                  | deaths<br>among these | Number<br>of cases | deaths<br>among these | Number<br>of cases | deaths<br>among these | Number<br>of cases | deaths<br>among these | Number<br>of cases | deaths<br>among these | Number<br>of cases | deaths<br>among these | Number<br>of cases | deaths<br>among these | Number<br>of cases | deaths<br>among these | Number<br>of cases | deaths<br>among these | Number<br>of cases | deaths<br>among these | Number<br>of cases | deaths<br>among these |
| 18                                              | 7                     | 8                                                   | 3                     | 12                 | 1                     | —                  | —                     | 1                  | —                     | 39                 | 11                    | 6                  | —                     | 2                  | —                     | 2                  | —                     | —                  | —                     | —                  | —                     | 10                 | —                     |
| 15                                              | 4                     | 3                                                   | —                     | 8                  | —                     | 1                  | —                     | —                  | —                     | 27                 | 4                     | 1                  | —                     | 1                  | —                     | 1                  | —                     | —                  | —                     | —                  | —                     | 3                  | —                     |
| 9                                               | —                     | 3                                                   | —                     | 7                  | 2                     | 1                  | —                     | 3                  | —                     | 23                 | 2                     | 2                  | —                     | —                  | —                     | 2                  | 1                     | —                  | —                     | —                  | 1                     | 5                  | 1                     |
| 4                                               | —                     | 5                                                   | 1                     | 7                  | —                     | 4                  | 1                     | —                  | —                     | 20                 | 2                     | 1                  | —                     | 1                  | —                     | 4                  | —                     | —                  | —                     | —                  | —                     | 6                  | —                     |
| 8                                               | —                     | 3                                                   | —                     | 3                  | —                     | 2                  | —                     | 1                  | —                     | 17                 | —                     | 4                  | —                     | 2                  | —                     | —                  | —                     | —                  | —                     | —                  | —                     | 7                  | —                     |
| 3                                               | 1                     | 4                                                   | —                     | 7                  | —                     | 1                  | —                     | 1                  | —                     | 16                 | 1                     | 6                  | —                     | 2                  | —                     | 2                  | —                     | —                  | —                     | —                  | —                     | 10                 | —                     |
| 4                                               | —                     | 1                                                   | 1                     | —                  | —                     | —                  | —                     | 2                  | —                     | 7                  | 1                     | 4                  | —                     | 2                  | —                     | 1                  | —                     | —                  | —                     | —                  | —                     | 7                  | —                     |
| 5                                               | —                     | 5                                                   | 1                     | 9                  | 2                     | —                  | —                     | —                  | —                     | 22                 | 3                     | 18                 | 2                     | 6                  | —                     | 10                 | —                     | 1                  | —                     | —                  | 3                     | 38                 | 2                     |
| > 1 week                                        | —                     | —                                                   | 6                     | 53                 | 5                     | 9                  | 1                     | 11                 | —                     | 171                | 24                    | 42                 | 2                     | 16                 | —                     | 22                 | 1                     | 2                  | —                     | —                  | 4                     | 86                 | 3                     |
| Total                                           | 66                    | 12                                                  | 32                    | 6                  | 5                     | 9                  | 1                     | 11                 | —                     | 171                | 24                    | 42                 | 2                     | 16                 | —                     | 22                 | 1                     | 2                  | —                     | —                  | 4                     | 86                 | 3                     |

1931, it is 18.8 per cent (18 deaths among 96 patients), and for the years 1932—1935 it is 3.5 per cent (2 deaths among 58). The difference in mortality is statistically significant ( $\text{diff.} = 15.37 \pm 4.65$ ).

We may point out, that there is a certain amount of confusion as to the conception of interval. Some writers hold that the stage of interval in the disease means the stage in which the most acute symptoms have subsided, others refer to it as the stage in which the clinical symptoms have disappeared and the patient's temperature is normal; others think, on the other hand, that the stage of interval is the stage in which the morbid changes are also healed. In the case of acute cholecystitis, in which the patho-anatomical changes only slowly recede — it takes weeks or months — it might be of practical value to employ the term '*clinical interval*' in order to designate the stage of the disease in which the temperature has become normal, abdominal symptoms and possibly jaundice have disappeared, and the patient may be allowed out of bed.

Table 35 shows the material divided according to the stage of the disease in which the operation was performed. a) means that the patient was operated on on acute indication, i. e. early during the acute attack and because the symptoms were considered to be alarming, p) means that the patient was operated on while the attack was in progress but not until the most acute symptoms had subsided, and i), finally, means that the patient was operated on in the clinical interval. The material is further grouped in mild, medium-severe, and severe cases.

It is seen in the table that mild cases in the earliest period (1922—1927) were operated on both while the attack was in progress and in the clinical interval; since 1928, almost all of them were operated on in the clinical interval (on account of doubtful diagnosis 2 cases were operated on while the attack was still in progress).

The majority of the medium-severe cases were up to the year 1931 operated on while the attack was in progress; since 1932, practically all of them were operated on in the clinical interval.

Fifty per cent of the severe cases were during the years 1922—1931 operated on in an acute stage, and only a few in the clinical interval. In the years 1932—1935, on the other hand, half the number were operated on in the clinical interval, and less than fifty per cent in the acute stage.



The table also shows that the majority of the deaths occurred among the severe cases which were operated on in the acute stage or while the attack was in progress.

The above analysis of our material shows that in the years 1932—1935, a statistically significant decrease in mortality was present among the cases operated on. We have examined various possibilities in order to explain this decreased mortality. We have found that it cannot be explained by any change in the material of cholecystitis available, or by any selection of the patients operated on in order to obtain a prognostically more favourable material of operation. We have further pointed out that improvements in the technique of operation, particularly with regard to anesthesia and the treatment of the patients before and after the operation, may have contributed to lessen the mortality. Finally, we have been able to state that the indications for operation have changed in so far as, in the years 1932—1935, the patients were operated on in a later stage than previously and that, so far as possible, attempts were made to operate on the patients in the clinical interval. This change in the indications for operation have naturally also contributed to a comparatively larger number of the patients not being operated on.

It is naturally possible that factors other than the ones here analysed may also be important to the decreased mortality. In solving a scientific problem we must always reckon with the possibility that unknown factors which will only be revealed by the researches of later workers may play a certain part. A conclusion must always be reached on the basis of the knowledge at our disposal. In summing up we may maintain that an improved general technique has possibly been important. However, we are here hardly concerned with more obvious displacements, and under such circumstances we have reason to believe that the altered indications for operation to the effect that operations were in a large number of cases postponed until the stage of clinical interval, have played a fundamental part. If we want to be more cautious still, we may content ourselves by saying that a postponement of the operation until a stage of clinical interval has not increased the risk for the patient. In point of fact, if a postponement of the operation carries with it risks on account of the disease developing in a fatal direction, this should result in a) the patient being operated on under more unfavourable conditions than is necessary,



b) the situation being in some cases considered to be so hopeless that no operation is performed. On account of this we should expect that if cases developing in this direction are frequent, the mortality would increase either among those operated on, or among those not operated on, or among both categories. It is therefore important in this connection to point out that the cases not operated on present no increased mortality, either. The mortality is practically unchanged. Attention should further be called to the fact that a detailed analysis of deaths occurring among the patients not operated on, has led us to believe that in all probability none of these cases could have been saved by an earlier operation.

It is of great interest to be able to compare our material with those published by other authors. The only material so far published which is wholly comparable, is the one presented by LIEBERG (1937). This material is made up of all the cases of acute cholecystitis treated in the surgical clinic of Lund during the years 1923—1934, both those operated on and those not operated on, 556 in number. LIEBERG finds that the mortality after cholecystectomy in the earlier 5 years of the period during which the material was collected, was lower than in the subsequent 5 years. According to LIEBERG, this decreased mortality in the last 5-year group cannot be explained by the fact that in a larger number of grave cases, cholecystostomy only was performed, or by the fact that a smaller number of severe cases were operated on at all. In the following treatment of the material, no distinction is made between that part of the material which refers to the earlier years and the part referring to the later period. In order to be able to analyse the material from Lund in the same manner as we have analysed our own material, we had to divide the Lund material — on the basis of the case histories published — into two groups, one covering the years 1924—1928 and the other the years 1929—1935. We have further divided both the cases operated on and the cases not operated on according to age. In LIEBERG's collocation of the cases operated on, the diary numbers are stated. On the basis of the case reports we were therefore able to distribute these cases among the various year groups and also according to the more or less severe grade of the disease. For the cases not operated on, no data are given as to how they are distributed among the various year groups with regard to the grade of the disease.

The post-operative mortality in the material from Lund for all the operations carried out for acute cholecystitis, i. e. both cholecystectomy, and other operations (incision etc.) amounted to 11,4 per cent (308 cases with 35 deaths). In the years 1924—1928, it was 17,3 per cent and in the years 1929—1933, it was 5,6 per cent. The difference is statistically significant (diff. =  $11,7 \pm 3,7$ ). As, however, in our material we have neither included the cases in which stone was absent nor the cases with stone in the common bile duct, we have to remove these from the Lund material in order to be able to compare it with our material. In the material from Lund there were 13 cases (with 2 deaths) in which stone was not found. Further, in 20 cases stone in the common bile duct was found at operation<sup>1)</sup> or post-mortem examination, 7 of which died. Of the remaining 275 cases, 26 died (9,5 per cent). In the years 1924—1928, the mortality was 11,9 per cent, in the years 1929—1933, it was 6,5 per cent. The difference is statistically not probable (diff. =  $5,4 \pm 3,4$ ). The lower mortality in the entire Lund material of cases operated on during the years 1929—1933 thus may be largely explained by the fact that in the earlier material are included 10 cases of stone in the common bile duct, of which no less than 7 died. (In 3 cases, cholecystectomy was performed, in 2 cases cholecystostomy, and in 2 cases another operation.) If these cases had been included in the material from Lund, only the cases without stone being removed, the mortality for the years 1924—1928 would have been 16,5 per cent, and for the years 1929—1933, 6 per cent. The difference is statistically probable (diff. =  $10,5 \pm 3,6$ ). If to our material of cases operated on for acute cholecystitis we add the cases in which stone in the common bile duct was found at operation or post-mortem examination (25 cases), the mortality figure for our material is 15,0 per cent during the years 1922—1931, and 3,2 per cent during the years 1932—1935. The difference is statistically significant (diff. =  $11,8 \pm 3,2$ ). Even if, in our material, we include the cases presenting cholecystitis plus stone in the common bile duct, we thus find a statistically significant difference in the mortality.

<sup>1)</sup> Here is referred only to the first operation performed on a patient. On account of this, 2 cases in the material from Lund were not counted as cases of stone in the common bile duct, Nos. 196 and 470. In both these cases, cholecystostomy was first performed, and during a subsequent stay in hospital, cholecystectomy plus choledocholithotomy, and laparotomy plus drainage. Both patients died.

In the material from Lund, 64,9 per cent of all cases of acute cholecystitis were operated on during the years 1924—1928, and 42,4 per cent during the years 1929—1933. If we do not include the cases without stone and the cases with stone in the common bile duct, the corresponding percentage figures are 63,3 per cent and 39,7 per cent. — In the following discussion we shall only treat the cases in the material from Lund in which, so far as is known, neither absence of stone nor stone in the common bile duct occurred. — While a smaller part of the material was operated on, the total material presented an increase in number: during the earlier 5 years it consisted of 229 cases, during the subsequent 5 years of 295 cases. In Lund, just as in Uppsala, the acute cases of cholecystitis have been operated on to a smaller extent than formerly, in spite of the fact that the material of acute cholecystitis available has increased. The difference between the percentage of cases operated on in Lund during earlier and later years is greater than in Uppsala (23,7 per cent as against 9,4 per cent). We shall try to form an idea as to whether the material of cholecystitis in its entirety as well as the cases not operated on and the cases operated on have presented any changes in regard to age distribution and the more or less severe grade of the disease.

Table 36. *The material of acute cholecystitis from Lund: total material. Distribution according to age, at first stay in hospital, of cases not-operated on and cases operated on in the years 1924—1928 and 1929—1933.*

| Age,<br>years | 1924—1928          |                                |                    |                         |                    |                          | 1929—1933          |                                |                    |                         |                    |                          |
|---------------|--------------------|--------------------------------|--------------------|-------------------------|--------------------|--------------------------|--------------------|--------------------------------|--------------------|-------------------------|--------------------|--------------------------|
|               | Not operated       |                                | Operated           |                         | Not op. + op.      |                          | Not operated       |                                | Operated           |                         | Not op. + op.      |                          |
|               | Number<br>of cases | % of<br>cases<br>not op.<br>on | Number<br>of cases | % of<br>cases<br>op. on | Number<br>of cases | % of<br>not op.<br>+ op. | Number<br>of cases | % of<br>cases<br>not op.<br>on | Number<br>of cases | % of<br>cases<br>op. on | Number<br>of cases | % of<br>not op.<br>+ op. |
| Under 20      | —                  | —                              | 1                  | 0,7                     | 1                  | 0,4                      | 3                  | 1,7                            | —                  | —                       | 3                  | 1,                       |
| 20—29         | 1                  | 1,2                            | 12                 | 8,3                     | 13                 | 5,7                      | 5                  | 2,8                            | 11                 | 9,4                     | 16                 | 5,                       |
| 30—39         | 8                  | 9,5                            | 25                 | 17,2                    | 33                 | 14,4                     | 9                  | 5,1                            | 18                 | 15,4                    | 27                 | 9,                       |
| 40—49         | 14                 | 16,7                           | 37                 | 25,5                    | 51                 | 22,3                     | 25                 | 14,0                           | 30                 | 25,5                    | 55                 | 18,                      |
| 50—59         | 14                 | 16,7                           | 44                 | 30,4                    | 58                 | 25,3                     | 46                 | 25,8                           | 29                 | 24,8                    | 75                 | 25,                      |
| 60—69         | 31                 | 36,8                           | 17                 | 11,7                    | 48                 | 21,0                     | 43                 | 24,2                           | 25                 | 21,4                    | 68                 | 23,                      |
| 70—79         | 14                 | 16,7                           | 9                  | 6,2                     | 23                 | 10,0                     | 36                 | 20,2                           | 3                  | 2,6                     | 39                 | 13,                      |
| 80—89         | 2                  | 2,4                            | —                  | —                       | 2                  | 0,9                      | 11                 | 6,2                            | 1                  | 0,9                     | 12                 | 4,                       |
| Total         | 84                 | 100,0                          | 145                | 100,0                   | 229                | 100,0                    | 178                | 100,0                          | 117                | 100,0                   | 295                | 100,                     |

In table 36 the material from Lund is arranged according to the age at the first stay in hospital. The table shows that in more recent years, the older subjects were somewhat more represented among the cases not operated on, whereas the cases operated on show no changes to speak of in regard to age.

In regard to the grade of the disease, data are available, showing that 16 out of the cases not operated on were severe; of these, 5 belonged to the earlier group and 11 to the later group. As regards the medium-severe and mild cases, no information is given as to their distribution among the different year groups. In table 37 the cases operated on are distributed according to the grade of the disease. It shows that the material has not changed to any degree worth mentioning in this respect. We consequently find that the material from Lund, in agreement with our material, has shown an increase in number in recent years, but that this increase of the material has not involved any marked changes in the general composition of the material.

So far as is known, no important changes in the technique of operation, particularly in regard to the anesthesia, have occurred in Lund.

In table 38, the material from Lund of cases operated on is brought together and divided according to the time, as related to the beginning of the acute attack, at which the operation was performed and also into the 2 abovementioned periods, 1924—1928 and 1929—1933. The table shows that during the first 4 days of the disease, 45 per cent of the patients were operated on in the early period, and 46 per cent in the later period. During the 5th day, 53,6 per cent were operated on in the earlier period,

Table 37. *The material of acute cholecystitis from Lund: cases operated on during first stay in hospital. Grouping according to grade of disease.*

| Grade of disease          | 1924—1928       |                | 1929—1933       |                |
|---------------------------|-----------------|----------------|-----------------|----------------|
|                           | Number of cases | % of all cases | Number of cases | % of all cases |
| Mild cases .....          | 32              | 22,1           | 36              | 30,8           |
| Medium-severe cases ..... | 74              | 51,0           | 48              | 41,0           |
| Severe cases .....        | 39              | 26,9           | 33              | 28,2           |
| All cases .....           | 145             | 100,0          | 117             | 100,0          |



Table 38. *The material of acute cholecystitis from Lund: all cases operated on in 1924—1928 and 1929—1933. Cumulative distribution according to length of interval between beginning of attack and operation.*

| Interval between<br>beginning of attack<br>and operation | 1924—1928          |                          | 1929—1933          |                          |
|----------------------------------------------------------|--------------------|--------------------------|--------------------|--------------------------|
|                                                          | Number<br>of cases | % of total<br>year group | Number<br>of cases | % of total<br>year group |
| 0—1 day .....                                            | 10                 | 6,6                      | 7                  | 5,6                      |
| 0—2 days .....                                           | 30                 | 19,9                     | 22                 | 17,7                     |
| 0—3 » .....                                              | 53                 | 35,1                     | 43                 | 34,7                     |
| 0—4 » .....                                              | 68                 | 45,0                     | 57                 | 46,0                     |
| 0—5 » .....                                              | 81                 | 53,6                     | 60                 | 48,4                     |
| 0—6 » .....                                              | 89                 | 58,9                     | 65                 | 52,4                     |
| Within 1 week .....                                      | 99                 | 65,6                     | 71                 | 57,3                     |
| » 2 weeks ...                                            | 127                | 84,1                     | 96                 | 77,4                     |
| » 3 » ...                                                | 137                | 90,7                     | 109                | 87,9                     |
| Total                                                    | 151                | 100,0                    | 124                | 100,0                    |

and 48,4 per cent in the later period; during the 6th day 58,9, respectively 52,4, per cent of the patients. Consequently, only a slight change has occurred in regard to the time at which the operation was performed to the effect that after the 4th day of the disease operations were performed to a somewhat smaller extent during the years 1929—1933 as compared to the earlier period. If we compare this table with table 30, in which our own material is arranged in like manner, we find that the material from Lund as regards the time of operation tallies fairly closely with our own material during the years 1922—1931. In the years 1932—1935, our material, as pointed out above, shows that a considerably smaller number of patients were operated on during the first days of the disease, and further, that only 40 per cent of them were operated on during the first week of the disease.

As intimated above, it is a very hazardous matter to draw conclusions from figures relating to materials of operations. Two materials may present disparities in so many respects that it is difficult to decide what is the cause of a possible difference in the figures. So far as we have been able to go into the matter, the materials from Lund and Uppsala are comparable in regard to age distribution and the more or less severe grade of the disease in so far as this

may be estimated on the basis of the data given. We must remember, however, that the mortality in a material of operations in a disease like the one here under discussion, to a certain degree is related to the extent to which very severe cases are operated on. In a material of acute cholecystitis there are always cases in which it is doubtful whether an operation is worth while, or if the case should be considered so desolate that an interference is meaningless. In view of this it should be pointed out that in Lund, 63.3 per cent of the acute cases of cholecystitis were operated on during the first period, and only 39.7 during the second period. In Uppsala, on the other hand, the percentage of operations shows a smaller displacement; in the first period 47.0 per cent were operated on, and in the second period 37.6 per cent of the cases. In the material from Uppsala the difference is not statistically significant, but this is the case in the material from Lund (diff. in the Uppsala material =  $9.4 \pm 4.3$ ; diff. in the Lund material =  $23.7 \pm 4.3$ ). This being so, it might possibly be suspected that the displacement in the mortality which may be thought to be present in the material from Lund, is related to modified indications for operation. Such a possibility is very important in this connection, because a displacement which also involves a displacement in the indications, may fundamentally influence the mortality, when the very serious cases are operated on. Now it must be pointed out, however, that the difference in the mortality figures relating to the early and the later period which is present in the material from Lund, is not statistically significant. Under such circumstances it is not necessary to point to factors of this type in order to obtain an explanation of the figures. The displacement might well be determined by chance. In order to illustrate the part played by random variations it should further be pointed out that the absence of a statistically significant difference cannot be related to an unequal order of magnitude of the materials. (151, respectively 124 cases during the two periods with a mortality of 11.9 and 6.5 per cent, as against 171, respectively 86 cases in our material with a mortality of 14.0 and 3.5 per cent).<sup>1)</sup> Actually, the material from Lund is somewhat larger than the material from Uppsala for the latter period. As the material for this period is smallest in the Uppsala material, we have a better chance

<sup>1)</sup> In the Lund material of cases operated on are included 13 cases which were not operated on during their first stay in hospital.

of obtaining a significant difference in the material from Lund than in the material from Uppsala (regard being paid also to the size of the material from the early period).

If we assume that the percentage figures for the mortality found in our material, also refer to the material from Lund, and calculate the difference between them for the different periods of time, we find that it is  $10,5 \pm 3,2$ . The difference would accordingly be statistically significant in the material from Lund, if conditions had been the same in that material as in ours. The mortality figure for the early period in our material is higher than that referring to the early period of the material from Lund. If we therefore assume that the mortality in the material from Lund is unaltered during the early period but during the later period is the same as the one applying to our material, we arrive at a statistically probable difference (diff. =  $8,4 \pm 3,0$ ). If, on the other hand, we assume that the material from Lund in the early period presents the same mortality as that applying to the early period in our material, but on the other hand its own mortality for the later period, the difference would not be statistically significant, or even probable (diff. =  $7,5 \pm 3,6$ ). If, finally, we include cases with common duct stone both in the material from Lund and in our own material, assuming that the percentage figures for the mortality which were found in our material, are also present in the material from Lund, we arrive at a difference of  $11,8 \pm 3,2$ . In this case, also, the difference in mortality between the different periods of time would have been significant in the material from Lund, provided that the same conditions had prevailed there as in our material.

A statistical comparison might also be carried out in another manner. Instead of comparing the differences in the two materials we compare the primary and final figures. We find that there is no significant difference between the mortality figures for the materials from Uppsala and Lund for the early period, on one hand, and the corresponding figures for the materials from Uppsala and Lund for the later period, on the other (diff. =  $2,1 \pm 3,2$ , respectively  $3,0 \pm 3,0$ ). Theoretically, the figures may be interpreted in two ways. It might be that in Uppsala there is an actual difference between the two periods, whereas in the Lund material the difference is determined by chance. Against the background of the comparison carried out above, we might, however, also conceive of the

possibility that the difference between the materials from Uppsala and Lund are determined by chance for the earlier period, and that the same is true as regards the later period. In theory, both interpretations are possible but both cannot be correct. It is, however, at any rate certain that there is a difference which is not determined by chance between the two periods in the material from Uppsala. If the differences between the materials from Uppsala and Lund for both the early and the later period are considered to be determined by chance, an equally significant difference would also be present in the material from Lund.

In so far as we may estimate the situation for the Uppsala material of which the present author has a more detailed knowledge, the difference must in all probability here be referred to the altered indications for operation. All attempts to arrive at another explanation have failed. In view of the very great difficulties of comparing operation materials, generally, we must, however, admit of the possibility that unknown factors have played a part and that it is comparatively indifferent whether an operation is performed in an earlier, or later, stage of the disease. Even if we grant that, in interpreting operation materials, we must always pay due regard to the mystery of the unknown, it should on the other hand be considered that we are literally speaking concerned with a matter of life and death and that, consequently, we must act according to what seems most probable. Scientifically, the evidence is thus not quite conclusive, but we have, for the Uppsala material, valid reasons to refer the displacements to the altered indications for operation and to recommend the latter, the more so as it seems reasonable to expect that operation in a clinical interval should involve a smaller risk than operation during an acute stage.

If we want to maintain that the difference in the material from Lund is also real but that, owing to a random variation in the figures, the difference is not statistically significant, at any rate we can not assert that the explanation is to be sought in altered indications for operation of the same type as in Uppsala. This does not prevent that in Lund, also, altered indications for operation may have played a part. We have above suggested that the altered frequency of operation may be related to a modification of the indications and that to a larger extent operations are avoided in severe cases. In that case, we should, however, expect a higher mortality among the



cases not operated on in the material from Lund. Such an increase is not to be found and in so far as we have been able to estimate the more or less severe grade of the cases, such a difference does not seem to be present. The possibility remains, however, that an unknown factor has played a decisive part both in the material from Lund and in the material from Uppsala. No criteria in support of such a statement are present, however. Under such circumstances the most probable conclusion is that we have a real difference in the material from Uppsala which is probably related to the altered indications for operation, whereas the difference in the material from Lund is determined by chance. It must be emphasized, however, that this is only the most probable interpretation of the figures. Scientifically speaking, it is not fully proved. In the treatment of cases of disease we cannot wait until we have absolute certainty. We must act on the basis of probabilities. Similarly, in laying down general rules for our line of action, we should build on what seems to be most probable when we cannot arrive at full certainty. It should perhaps be emphasized that we look at this matter solely from the point of view of the death-risk incurred by the patients relative to the operation, as this viewpoint preponderates over all other considerations.<sup>1)</sup>

The fact is, however, that we are not justified in all cases of acute cholecystitis to postpone a possible operation until the acute symptoms have subsided. In a material of cholecystitis are found a far from small number of patients who have the disease in such a severe grade with a considerably affected general state of health and pronounced local symptoms, that we are forced to operate, irrespectively of the time elapsed after the beginning of the attack. Before discussing this problem more closely, we shall however briefly describe our material in regard to the death-risk at different ages, for men and for women.

It is chiefly after Horz in 1923 published a very large tabulation of cases operated on for gall stone disease that we know that operation for gall stone disease involves a considerably greater risk for older, than for younger, persons. In table 35 the patients are grouped according to age under 50 and age over 50. For the total

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<sup>1)</sup> If other points of importance to the indications for operations were also to be discussed, we should have to pay regard to the short time of hospital treatment for those who were operated on in an early stage, etc.

material, the mortality for patients under 50 is 5,2, and for patients over 50 it is 16,3 per cent. The difference is statistically probable (diff. =  $11,1 \pm 3,8$ ). For the years 1922—1931, the corresponding figures are 7,9 per cent and 20,7 per cent, with a statistically not probable difference (diff. =  $12,8 \pm 5,3$ ), and for the years 1932—1935, 0 per cent, respectively 16,7 per cent, with statistically significant difference (diff. =  $16,7 \pm 5,6$ ). The lastmentioned material, however, is comparatively small in this respect. The percentage mortality for the total material, divided into age classes, appears in table 26. It is principally for the ages over 60 that the mortality increases.

Horz pointed out that the mortality in men is considerably higher than in women, and in his large material obtained conclusive figures: for simple cholecystectomy, with or without drainage, the mortality was 15,03 per cent for men (251 deaths among 1.670 operations), and 7,34 per cent for women (674 deaths among 9.178 operations). These figures refer both to cases of acute cholecystitis and of non-complicated gall stone disease. In our material of acute cholecystitis, 8 out of 40 men died (20 per cent), and 19 out of 217 women (8,8 per cent). The difference in mortality is not statistically probable (diff. =  $11,2 \pm 6,6$ ). There are comparatively few men in our material. As the percentage difference in mortality is considerable, it is possible that a larger material would yield a statistically significant difference in mortality for men as compared to women.

The question arises as to what may be the cause of the higher mortality among men, which has been demonstrated in other materials. In our material of cases operated on for acute cholecystitis the men are not more represented in the higher age classes than in the lower. 52,5 per cent of the men were over 50 years of age, and 47,0 per cent of the women (diff. =  $5,5 \pm 8,6$ ). We find (see table 39) that a relatively larger part of the men had cholecystitis in a severe form (17 men out of 40, i. e. 42,5 per cent; 63 women out of 217, i. e. 29 per cent). The difference is not statistically probable (diff. =  $13,5 \pm 8,4$ ). As the percentage difference is comparatively great and as the material of men operated on is small, it is possible that a larger material might yield a statistically significant difference in this respect. We have given the above data on our material for the reason that it is conceivable that materials

Table 39. *All cases of acute cholecystitis operated on in 1922—1935. The material distributed according to age at operation, sex and grade of disease.*

| Age at operation, years | Mild cases      |                    |                 |                    | Medium-severe cases |                    |                 |                    | Severe cases    |                    |                 |                    | All cases       |                    |                 |                    |
|-------------------------|-----------------|--------------------|-----------------|--------------------|---------------------|--------------------|-----------------|--------------------|-----------------|--------------------|-----------------|--------------------|-----------------|--------------------|-----------------|--------------------|
|                         | Men             |                    | Women           |                    | Men                 |                    | Women           |                    | Men             |                    | Women           |                    | Men             |                    | Women           |                    |
|                         | Number of cases | deaths among these | Number of cases | deaths among these | Number of cases     | deaths among these | Number of cases | deaths among these | Number of cases | deaths among these | Number of cases | deaths among these | Number of cases | deaths among these | Number of cases | deaths among these |
|                         |                 |                    |                 |                    |                     |                    |                 |                    |                 |                    |                 |                    |                 |                    |                 |                    |
| 20—24                   | —               | —                  | 1               | —                  | —                   | —                  | 1               | —                  | —               | —                  | 1               | —                  | —               | —                  | 3               | —                  |
| 25—29                   | —               | —                  | 6               | —                  | —                   | —                  | 7               | —                  | —               | —                  | —               | —                  | —               | —                  | 13              | —                  |
| 30—34                   | 2               | —                  | 3               | —                  | 1                   | —                  | 11              | —                  | —               | —                  | 6               | 1                  | 3               | —                  | 20              | 1                  |
| 35—39                   | —               | —                  | 12              | —                  | 2                   | 1                  | 12              | —                  | 1               | —                  | 6               | —                  | 3               | 1                  | 30              | —                  |
| 40—44                   | 1               | —                  | 2               | —                  | 4                   | —                  | 14              | 1                  | 3               | 1                  | 4               | —                  | 8               | 1                  | 20              | 1                  |
| 45—49                   | 1               | —                  | 4               | —                  | 3                   | —                  | 17              | 2                  | 1               | 1                  | 8               | —                  | 5               | 1                  | 29              | 2                  |
| 50—54                   | —               | —                  | 1               | —                  | 4                   | —                  | 28              | 1                  | 4               | 1                  | 8               | 2                  | 8               | 1                  | 37              | 3                  |
| 55—59                   | —               | —                  | 2               | —                  | 2                   | —                  | 9               | 1                  | —               | —                  | 4               | —                  | 2               | —                  | 15              | 1                  |
| 60—64                   | —               | —                  | 3               | —                  | 1                   | —                  | 8               | 1                  | 3               | —                  | 13              | 8                  | 4               | —                  | 24              | 9                  |
| 65—69                   | —               | —                  | 1               | —                  | 2                   | —                  | 9               | —                  | 3               | 2                  | 7               | 1                  | 5               | 2                  | 17              | 1                  |
| 70—74                   | —               | —                  | —               | —                  | —                   | —                  | 2               | —                  | 1               | 1                  | 4               | —                  | 1               | 1                  | 6               | —                  |
| 75—79                   | —               | —                  | —               | —                  | —                   | —                  | 1               | —                  | 1               | 1                  | 2               | 1                  | 1               | 1                  | 3               | 1                  |
| Total                   | 4               | —                  | 35              | —                  | 19                  | 1                  | 119             | 6                  | 17              | 7                  | 63              | 13                 | 40              | 8                  | 217             | 19                 |

with a higher mortality for men also show that men to a greater extent are affected with the disease in a severe form. There are data showing that other acute abdominal diseases also involve a higher mortality for men and this on account of the fact that a larger number among the men have the disease in a more severe form than the women. NYSTRÖM (1919), for instance, has shown in a material of appendicitis that the mortality among men was higher than among women and that this was due to the fact that the men to a greater extent than the women had the disease in a severe form: the cases of peritonitis were more numerous among the men than among the women.

We have pointed out above that in a large number of cases of acute cholecystitis we need not operate immediately, but may stand expectant until the clinical symptoms have abated. It is naturally difficult to decide how large is the number of such cases in a material of cholecystitis. In gauging the indications for operation in an acute stage we have ascribed a fair importance not only to the

patient's general condition but also to the extension of the peritonitis which is always to be found in these cases. If the symptoms of peritonitis are limited to the upper portion of the abdomen and do not reach below the umbilical plane, we have in most cases considered it justified to stand expectant. In the cases, on the other hand, in which the peritoneal irritation has spread over a larger portion of the abdomen, we have thought that indication for operation is present.

The grave cases in which we have considered it necessary to operate in an early stage of the disease, that is to say on acute indication, in the later period consisted of about  $\frac{1}{3}$  of the grave cases (11 out of 31). For the severe cases, the risk of dying is great, whether an operation is performed or not. Many authors hold that in such grave cases only *cholecystostomy* ought to be performed, (e. g. ANSCHÜTZ, BRUGGEMAN, CAVE, PETRÉN, SOUPAULT and THALHEIMER, WILKIE). This operation is considerably less complicated than cholecystectomy and may be performed under local anesthesia.

It has been objected that cholecystostomy involves a considerably greater risk of relapse than cholecystectomy. There are, however, collocations which indicate that the risk of relapse after cholecystostomy is not very great. Of ROVSING's 302 cases, 280 were healthy at the time of a re-examination. MOORE found that 40 per cent of the cases of cholecystostomy were healthy 3—10 years after the operation, and DIETERICH, who re-examined 48 cases, found 33 to be free from symptoms. It might also be imagined that the risk of relapse after cholecystostomy, in which it is as a rule possible to remove the stones from the gall bladder, will be less than the one applying to patients not operated on. We have in a foregoing chapter (ch. 4) dealt with the risk of relapse for the patients not operated on. For the total material it was 47,5 per cent. For those who had had only one or two attacks, it was 35,4 per cent, and for those who had had more than two attacks, it was 67,1 per cent. Out of the 38 patients with severe acute cholecystitis who in our material had been operated on during the acute seizure, 16, i. e. almost 50 per cent, had had 2 attacks at most. We are thus justified in counting with the fact that a comparatively large number of the patients, who need be operated on for severe acute cholecystitis, are in a stage of disease in which the risk of relapse is comparatively small, even if they are not operated on.



We may thus assume that the risk of relapse after cholecystostomy will in these cases be comparatively small. When we are concerned with the most severe cases of acute cholecystitis, we have no particular reason, in the choice of method of operation, to pay special regard to the risk of relapse. The most important thing is to consider the actual risk of dying. Almost fifty per cent (34 out of 80) of the severe cases operated on in our material were over 60 years old. At this age, the risk of an operation is in itself greater than at younger ages. Of the 34 patients, 14 died. Of the patients under the age of 50 (46 in number), only 6 died. This speaks in favour of making the operation as little complicated as possible. In our opinion we have reason to rank the severe cases of acute cholecystitis in the same category as cases of perforated ulcer. As regards the treatment of perforated ulcer everybody seems to be agreed that it ought to consist of the simplest possible operation (suture of the ulcer). A radical operation is in these cases considered to be attended by a comparatively great risk.

Severe acute cholecystitis involves a comparatively great death-risk. Some patients are admitted in such a desolate condition that all therapy is of no avail. In our material these patients made up about 6 per cent of the cases not operated on. Others come to treatment with the disease in such a grave form that the risk of dying must be considered to be very great, but are on the other hand not in such a poor condition that the situation seems altogether hopeless. Such cases, as well as the cases in which a grave acute deterioration of the condition takes place during expectant treatment, ought to be operated on in the acute stage. In the severe acute cases in which the operation has to be performed during the acute stage, it naturally ought to be restricted to the simplest possible interference: cholecystostomy is then the operation that should be chosen. In the other cases we have reason to expect that the acute cholecystitis will improve spontaneously. Naturally, it would be most adequate not to operate on these patients until the inflammatory process in the gall bladder has actually healed. However, this is as a rule not possible (see p. 127). Operation in a stage of clinical interval, that is to say after the acute symptoms have subsided and the patient is able to be up and about, involves, according to what is shown in our material, a comparatively small risk.

### **Choledocholithiasis.**

An operation for stone in the common bile duct involves a comparatively great death-risk. In many tabulations of cases operated on for gall stone disease, the mortality applying to operation for common duct stone is higher than for other forms of the disease. The high mortality after operation for common duct stone is due to complications and changes brought about by such stones: hindrance to the passage of the bile by way of the common duct, accompanied by jaundice, inflammatory changes in the common duct and disturbances in the liver function.

Before discussing our own material, we shall give an account of the literature on this subject relating to the last decades, with regard to the post-operative mortality. In chapter I we pointed out that, in recent years, especially in the last decade, there has been a tendency to explore the common bile duct to a larger extent than previously in operations for gall stone disease. The conviction has gained ground more and more that stone may be present in the common bile duct without giving clinical symptoms. In gauging the risk involved in operation for common duct stone it is therefore necessary to try to distinguish between the cases in which common duct stone has given clinical symptoms, and those in which it was discovered more incidentally. To the former group we must refer the cases in which stone in the common bile duct has caused jaundice, cholangitis and disturbance in the liver function, that is to say the complications which are considered to be the cause of the high mortality in operation for common duct stone. In the literature, the abovementioned two groups of cases are as a rule not distinguished between. Further, the cases in which choledochotomy was performed and stone was found, are often brought together with the cases in which no stone was found. Finally, in some cases no distinction is made between the choledochotomies which were performed on the occasion of the patient's first operation, and operations for relapse subsequently made. As we here only deal with the first operation for gall stone disease performed on the patients in question, we have tried, when possible, to sort out the operations for relapse from the available materials of operation for common duct stone.

ROHDE (1920) in his material had 59 cases of common duct stone. 22 of these died after the operation (i. e. 37 per cent). Of the 59 cases, 14 had common duct hindrance without infection; of these 1 died. Of 23 cases, in which the common duct hindrance was attended by cholangitis, 3 died. The remaining 15 cases, of which no less than 12 died, were complicated by cholangitis, liver abscesses, peritonitis and sepsis.

If we bring together the last two groups of cases into one group, comprising the complicated cases of common duct stone, we get 38 cases, 15 of which died.

In 1921 HEIDENHAIN presented a material in which choledochotomy had been performed in 158 cases, with 23 deaths (i. e. 14,6 per cent). No information is given as to the percentage of those cases in which common duct stone was found, neither as to whether the material includes cases of operation for relapse.

In KASPER's material (1923) were found 67 cases with complicated choledocholithiasis. Of these, 10 died.

In the statistical survey published by HORTZ (1923) are found 1242 cases operated on in the acute stage, in which cholecystectomy and choledochotomy were performed. The mortality was 23 per cent (286 deaths). In the remission, 1758 analogous cases were operated on, with a mortality of 9,5 per cent (167 deaths). No information is given as to the number of cases in which stone was found in the common duct.

JUDD and PARKER (1926) had a material of 1115 cases operated on for disease of the biliary ducts. Among these were found 105 cases which had been operated on for stone in the common bile duct, with a mortality of 4,8 per cent (5 deaths).

ANSCHÜTZ (1927) reports on 258 choledochotomies. 70 of these were performed during the acute stage. Of 40 cases which presented jaundice but no fever, 10 died (i. e. 25 per cent) and of 30 which presented jaundice with fever, 12 died (i. e. 40 per cent). In another number of 30 cases choledochotomy was performed during the attack. These cases did not present jaundice. It is not stated whether stone in the common duct was found.

Among PEITMAN's (1926) 650 operations for gall stone disease were included 66 cases of choledochotomy with 10 deaths (i. e. 15,2 per cent).

In FLÖRCKEN's material (1926) were included 166 cases which

presented cholangitis, common duct stone, jaundice, liver changes, and pancreatitis. Of these 18 died (i. e. 10,8 per cent).

JUDD and WALTERS in 1929 reported on 1079 operations which in 1928 had been performed in the Mayo clinic for diseases of the gall bladder and biliary ducts. In this material were included 129 cases, operated on for stones in the gall bladder and common bile duct, with 6 deaths (i. e. 4,6 per cent).

WILKIE (1933) had 12 deaths among 130 cases operated on for stone in the common duct (i. e. 9,2 per cent).

In RANZI's (1934) material of 1031 cases operated on for gall stone disease, there were 150 in which supraduodenal choledochotomy had been performed, with 29 deaths (19,3 per cent). In 58 cases, transduodenal choledochotomy had been performed, with 16 deaths (i. e. 27,6 per cent). In all, 45 patients had died out of 208 cases in which choledochotomy had been performed (i. e. 21,6 per cent).

Out of 537 cases in ELIASON and ERB's material (1935), choledochotomy had been performed in 92 cases, 8 of which died (i. e. 8,7 per cent). In 54 out of the 92 cases, stone in the common duct had been found.

FINSTERER in 1935 reported on his material of 601 operations for gall stone disease. In 99 cases operation had been performed for common duct stone and cholangitis. 10 of these died.

LAHEY and SWINTON in 1935 published a material of common duct stones. Of 1800 cases operated on for gall stone, the common duct had been explored in 531 cases, i. e. in 30 per cent of the cases. In 258 cases common duct stone was found, i. e. in 14 per cent of the total material. The authors describe 221 cases more closely. Relative to the operation 7,6 per cent of these died. 39 per cent of the 221 cases had neither had jaundice in the anamnesis nor presented jaundice during the stay in the hospital. The material largely consisted of non-complicated cases; only 9 had chills and fever. No less than 15, or 7,4 per cent, of the cases were under the age of 30, and 46 per cent of the cases had had their symptoms over a shorter period than one year. The authors emphasize the importance of exploring the common duct in the cases, also, in which there is no direct cause for expecting that common duct stone is present. They formulated their indications for choledochotomy as follows: »Common and hepatic ducts should be explored in all jaundiced patients and in all patients in whom a reasonably recent history of jaundice is



present, in all patients with a markedly thickened or contracted gall-bladder since long-standing cholelithiasis and gall bladder infection make conditions so favorable for the production of duct stones and is so frequently associated with stones. We believe that the common and hepatic ducts should be opened and explored when the common duct is either thickened or dilated, particularly when the gall bladder has not previously been removed. We believe that the common and hepatic ducts should be opened and explored when any suspicious lump suggesting stone can be felt on palpation of the ducts between the palpating thumb and finger. We believe that the common and hepatic ducts should be opened and explored particularly in the presence of cholelithiasis or cholecystitis when the head of the pancreas is so thickened and indurated that stones at the ampulla of Vater within the thickened head of the pancreas could be overlooked. We believe that the common and hepatic ducts should be opened and explored when bile withdrawn into a hypodermic syringe, the needle of which has been passed into the duct, is not golden yellow in color and perfectly transparent and clear in character».<sup>1)</sup>

ALLEN (1936) reports on 1228 operations for gall stone disease. In 395 cases, choledochotomy was performed. 17 of these died (i. e. 4,4 per cent). In 167 cases common duct stone was found.

DEMEL (1936) had a material of 252 operations for gall stone disease. In 86 cases, choledochotomy had been performed for stone in the common duct. In 6 of these cases, cholecystectomy had previously been made, and in one case a gall fistula was found. DEMEL divided his material of choledochotomies according to the principles suggested by W. J. Mayo as early as 1906. The cases which had not had jaundice, had normal bile and no active symptoms, were referred to one group. 32 cases belonged to this group, one of which died. To another group were referred the cases which had active infection of the common duct with jaundice, chills and high temperature. 29 cases belonged to this group, with 3 deaths. Finally were brought into a third group the cases which had symptoms of complete obstruction in the common duct. DEMEL thought it wise to avoid, if possible, an operation in the acute feverish stage and try to wait until the temperature had decreased.

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<sup>1)</sup> We have quoted these authors because their indications for exploration of the common duct are the ones which at present seem to be fairly generally adopted.

BERNHARD in 1936 published a compilation of 1000 choledochotomies from the year 1895 up to 1932. The relation between choledochotomy and cholecystectomy was 1 to 5. Of the entire material, 9.9 per cent died. In the material were included 100 cases in which operation for relapse had been performed. In 185 cases, no stone in the common duct was found.

WILKIE (1937) had operated on 190 cases for stone in the common bile duct, 8.9 per cent of which died. In all the cases jaundice was present.

The review of the literature shows that the postoperative mortality in common duct stone is fairly high. Only in some materials is the mortality comparatively low (LAHEY and SWINTON, ALDEN). This may be related to the fact that in these materials a comparatively great percentage of fairly mild cases are included. In LAHEY and SWINTON's material, for instance, only a small number of the patients had infection of the biliary ducts. Many of the patients were comparatively young or had been ill during a short period.

We have pointed out above that the composition of a material of patients with common duct stone may be of decisive importance to the magnitude of the post-operative mortality. The risk involved in an operation is smaller in the cases in which common duct stone is found without having given clinical symptoms. The risk increases in the cases in which common duct stone has caused an obstruction of the common duct and possibly infection of the biliary ducts. In trying to obtain an idea of the risk of operation for common duct stone, we must try to divide the material into different groups.

Theoretically, we have to count with different possibilities in cases of common duct stone.

1) Common duct stone may be present without giving clinical symptoms, being discovered in operation for another form of gall stone disease (cholelithiasis or cholecystitis) incidentally or by cholangiography.

2) Common duct stone may be co-existent with another form of gall stone disease and give symptoms which may indicate stone in the common bile duct but yet may be caused by another form of gall stone disease or complications from other organs. We are here principally concerned with less severe forms of jaundice, which

have either been present in previous attacks or appear during the stay in the hospital. In acute cholecystitis mild jaundice is comparatively frequent, caused by a hepatitis which is co-existent with the cholecystitis. Jaundice may further be caused by acute lymphadenitis round the common duct, acute pancreatitis, etc.

3) Common duct stone may give isolated clinical symptoms in the form of jaundice or cholangitis, or both.

4) Co-existent with common duct stone which gives typical symptoms, we may find inflammatory changes in the gall bladder, as a more or less dominating feature of the clinical picture.

Even though, in theory, such a grouping is clear, that does not mean that, in practice, it is easy to differentiate the cases of disease. Obviously, there is no sharp border-line between the groups. It is, however, very important to try as far as possible to divide the cases of common duct stone in this or similar manner, in order to find out in what cases the risk of operation is greatest. Groupings of cases fairly similar to the one suggested above have been made by W. J. MAYO, 1906, and DEMEL, 1936.

In grouping our material we found that the theoretical classification given above was difficult to adhere to in practice. It proved to be especially difficult, among the cases which presented fever and symptoms of peritoneal irritation round the gall bladder, to distinguish between those in which these symptoms were due to acute cholecystitis, and those in which they were due to inflammatory processes in the biliary ducts. We have therefore throughout made a division into three groups and distinguished between cases with and without fever, and from the cases with fever we have tried to differentiate the cases which presented acute cholecystitis, diagnosed in operation. The groups dealt with consequently are as follows:

1) Cases in which common duct stone did not give clinical symptoms but was incidentally discovered in operation for another form of gall stone disease or in later autopsy.

2) Cases in which the common bile duct was explored because there was cause for suspecting common duct stone on account of jaundice in the anamnesis or during the stay in the hospital, or owing to pancreatitis.

3) Cases with pronounced jaundice, with or without cholangitis.

Table 40. All cases of common duct stone, operated on. The material distributed according to different clinical groups and deaths.

| Clinical symptoms                     | Without fever |                    |       |                    |            |                    | With fever |                    |       |                    |            |                    |
|---------------------------------------|---------------|--------------------|-------|--------------------|------------|--------------------|------------|--------------------|-------|--------------------|------------|--------------------|
|                                       | Men           | deaths among these | Women | deaths among these | Both sexes | deaths among these | Men        | deaths among these | Women | deaths among these | Both sexes | deaths among these |
| <i>No clinical symptoms</i>           |               |                    |       |                    |            |                    |            |                    |       |                    |            |                    |
| Number of cases .....                 | 1             | —                  | 9     | —                  | 10         | —                  | —          | —                  | 8     | 1                  | 8          | 1                  |
| acute cholecystitis among these ..... | —             | —                  | —     | —                  | —          | —                  | —          | —                  | 6     | 1                  | 6          | 1                  |
| <i>Mild jaundice or pancreatitis</i>  |               |                    |       |                    |            |                    |            |                    |       |                    |            |                    |
| Number of cases .....                 | 4             | —                  | 11    | —                  | 15         | —                  | 3          | 4                  | 24    | 4                  | 27         | 4                  |
| acute cholecystitis among these ..... | —             | —                  | —     | —                  | —          | —                  | 1          | 1                  | 8     | 1                  | 9          | 1                  |
| <i>Common duct obstruction</i>        |               |                    |       |                    |            |                    |            |                    |       |                    |            |                    |
| Number of cases .....                 | 8             | 2                  | 12    | 1                  | 20         | 3                  | 3          | 4                  | 19    | 4                  | 22         | 6                  |
| acute cholecystitis among these ..... | —             | —                  | —     | —                  | —          | —                  | 1          | 2                  | 9     | 2                  | 10         | 2                  |



### Results of hospital treatment.

The clinical material includes 102 cases with common duct stone, of which 14 died relative to the operation (13,7 per cent). The distribution of the cases among the different abovementioned groups and the deaths in the groups appear in table 40.

#### I. *Cases with common duct stone incidentally discovered.*

##### A) Cases without fever:

In this group no deaths occurred.

##### B) Cases with fever:

Of the 8 patients 1 died.

1) 832/1928. Woman, aged 78. First attack, setting in the day prior to admittance.

Admitted on March 19. Very poor general condition. Temperature 38.2° C. Violent pains in the upper portion of the abdomen. Intense tenderness and rigidity in the right half of the abdomen and in the epigastrium. — In view of the patient's strongly affected general condition, expectant treatment was decided on. — In the evening of the day after admittance, severe abdominal pains suddenly set in and the temp. rose to 38.6° C. Immediate *cholecystostomy*. In the free peritoneal cavity clear bile. Round the gall bladder, under the lower surface of the liver, and between the liver and the diaphragm, thick, viscous pus was found. The gall bladder was largely gangrenous. Died 4 days later.

Autopsy: bronchopneumoniae; chronic purulent circumscribed peritonitis; acute gangrenous cholecystitis; choledocholithiasis. In the common duct were found two stones, the size of a hazelnut, above which the lumen of the passage was strongly dilated.

The expectant treatment must in this case be considered to have been unsuitable; whether, by an earlier operation, the aged patient could have been saved, seems doubtful, however.

In this case, in which only cholecystostomy was performed for the acute cholecystitis, common duct stone was discovered in the post-mortem examination.

#### II. *Cases in which, owing to clinical symptoms, there was cause for suspecting common duct stone.*

##### A) Cases without fever.

Of the 15 cases in this group none died.

## B) Cases with fever.

Of the 27 cases in this group 4 died.

One of the cases died from acute peritonitis.

2) 739/1928. Woman, aged 57. First attack one year previously, second attack 2 days prior to admittance.

Admitted on March 8. Strongly affected general condition. Jaundiced. Temperature 38.7° C. Marked tenderness on pressure all over the abdomen, particularly in its upper portion. Muscular rigidity corresponding to the tenderness. Immediate *cholecystectomy* and *choledocholithotomy by way of the cystic duct*. Narcosis. In the peritoneal cavity large amounts of bile. Gall bladder, the size of a dove's egg, with thickened, fibrin-covered wall. In the proximal part of the collum on the border-line of the cystic duct a perforation opening. In the common duct was found a stone, the size of the end of a thumb. In the gall bladder were found stones. — Died 3 days later.

Autopsy: bilateral mucopurulent bronchitis; bronchopneumoniae of the right lung; diffuse fibropurulent peritonitis. The biliary ducts were strongly dilated, but held no stones.

In the remaining three cases the immediate cause of death was acute pancreatitis.

3) 2087/1927. Woman, aged 41. Had had attacks both in 1918 and since 1926. For 10 days a dull pain in the pit of the stomach, radiating towards the back.

Admitted on Aug. 15. Slightly affected general condition. Mild jaundice. Temperature 37.7° C. Moderate tenderness and rigidity over the region of the gall bladder. The temperature rose to 38° C after 3 days. — Aug. 22. *Cholecystectomy* and *choledocholithotomy by way of the cystic duct*. Narcosis. The gall bladder small, the cystic duct half a little finger in width, filled with stones. The common bile duct was also filled with stones as far down as the papilla. *Preparation*: chronic and lithiasic cholecystitis (micr.). Stones in the gall bladder. Aug. 27. Vomiting. Acute dilatation of the ventricle. — Aug. 28. Blood transfusion. — Aug. 29. Died. No autopsy was made. In this case it might be supposed that either an acute liver insufficiency was present, or else — and maybe more probably on account of the rise of temperature up to 41.4° C before death and the abundant vomitings — that the patient had an acute pancreatitis.

4) 1853/1932. Woman, aged 64. For 35 years increasing dyspeptic complaints: vomitings and discomforts after meals. In 1905 a series of attacks of pain, as also the day before admittance to the hospital.

Admitted on July 15. Good general condition. Slightly jaundiced. Temperature 40° C. Tenderness in the epigastrium and over the region of the gall bladder. — After a week the patient was subfebrile. — Aug. 1. *Cholecystectomy* and *probing of the common duct*. Narcosis. Strongly shrivelled, thick and fixed gall bladder. The common duct dilated. No stones could be found in the latter. — Aug. 3. Sudden deterioration with circulation insufficiency and coma. Died the same day.

Autopsy: acute tracheobronchitis; fatty necroses of the pancreas; chole-  
docholithiasis; parenchymatous organic degeneration.

5) 416/1933. Woman, aged 55. Recurrent attacks for 8 years. Latest  
attack 3 days prior to admittance.

Admitted on Feb. 4. Good general condition. Not jaundiced. Tempera-  
ture 38.2° C. Tenderness over the region of the gall bladder. Diastase value  
in the urine: 512. — Feb. 5. Diastase value in the urine: at least 1024. —  
Feb. 6. Diastase value in the urine: 64. The temperature kept around 38° C.  
— Feb. 7. Cholecystectomy and choledocholithotomy  
by way of the cystic duct. Local anesthesia, narcosis. The gall  
bladder was the size of a pear, flushed and with strongly thickened walls. It  
contained clear, green bile. The common duct was pencil-wide. In its  
lower portion a few stones were found, the size of half a grain of rice. The  
edge of the liver considerably swollen and cyanotic. *Prep.*: the gall bladder  
mucosa was swollen, in the gall bladder an abundance of stones. — Feb. 8.  
Coffee-ground vomits. — Feb. 10. Deteriorated condition. Vomiting.  
Intravenous injection of invertose. — Feb. 11. Vessel collapse. The abdo-  
men taut. Tenderness round the wound.

Débridement of the wound. Died the same day.

Autopsy: circumscribed fibrinous peritonitis; chronic and acute pancreatitis.  
(Abundance of fatty necroses in the pancreas and in the rest of the abdomen);  
lipomatous myodegeneration of the heart; steatosis of the liver.

### III. *Cases with pronounced jaundice.*

#### A) Cases without fever.

Of the 20 cases in this group, 3 died.

One patient died from another disease.

6) 1113/1929. Man, aged 59. Had had 3 attacks during a time of 4 months.  
Latest attack 11 days before admittance. Jaundiced since the attack.

Admitted on April 29. Temperature 39° C. The abdomen soft, not tender.  
Pronounced jaundice. — May 1. Cholecystectomy and chole-  
docholithotomy by way of the cystic duct; drain-  
age of the common duct. The gall bladder was embedded in  
adhesions. The cystic duct was dilated. In the common duct turbid bile.  
From the vicinity of Vater's papilla a cement-resembling mass was collected.  
May 2. Sudden deterioration. Abdomen normal. During the last 24 hours a  
discoloration had rapidly spread from the sacral region. It was interpreted  
as a hematogenically developed, localized eruption of streptococci. — May  
3. Died from sepsis. No autopsy. — It is possible that the septic metastasis  
developed from the cholangitis.

In one of the remaining cases the immediate  
cause of death was an acute bronchitis; in  
the other possibly an acute liver insuffici-  
ency.

7) 1270/1926. Man, aged 48. Had had one attack every year for 5 years. The last three weeks recurrent attacks. Jaundiced.

Admitted on May 14. Good general condition. Jaundiced. Temperature  $37.5^{\circ}\text{C}$ . Some tenderness over the region of the gall bladder. — May 15. *Cholecystectomy; hepaticostomy; choledochotomy; drainage of the liver.* Narcosis. Shrivelled gall bladder, embedded in adhesions. Several remainders of abscesses were found. The extraduodenal portion of the common duct was surrounded by cartilaginous masses. The hepatic duct could be laid free and the common duct explored by way of the latter. No stone was found. *Prep.*: in the gall bladder an abundance of stones. — After the operation the jaundice disappeared in a few days. — June 30. The flow of bile from the wound has ceased almost altogether. The patient's condition increasingly worse. — July 9. Rise in temperature up to  $40^{\circ}\text{C}$ . Died.

Autopsy: bilateral purulent bronchitis; fistula fellae externa; choledocholithiasis; nephrosis. In the common duct a stone was found, well the size of a pea.

8) 2390/1926. Woman, aged 57. A number of attacks for 5 years. Several attacks combined with jaundice.

Admitted on Sep. 18. Affected general condition. Jaundice. Temperature  $38.2^{\circ}\text{C}$ . Liver and spleen enlarged, slightly tender. — Nov. 15. *Cholecystectomy and choledocholithotomy.* Local anasthesia and narcosis. The gall bladder thickened, surrounded by solid fibrous adhesions. It was broadly connected with the common duct. A number of stones were found in the common duct. Nov. 25. Confused, hallucinations. — Nov. 27. Stiff-necked. Lumbal puncture reveals normal pressure. No cells. Nonne was negative. Nov. 29. The patient's condition is getting worse, confused. Died. The temperature rose up to  $41.8^{\circ}\text{C}$  the last days.

Autopsy: tuberculous cavern of the right lung; myoma of the uterus. No obvious cause of death found in the post-mortem examination. The liver was enlarged in the autopsy, light in colour, without marked contours, the lobuli fatty. In spite of the absence of data on the quantities of urine after the operation it might be supposed that this was a case of liver insufficiency, with resulting coma.

## B) Cases with fever.

Of the 22 cases in this group, no less than 6 died.

One patient died from disease of the kidneys.

9) 2083/1930. Woman, aged 32. Treated in the hospital 2 months previously for the first attack — had acute cholecystitis with a temperature of at most  $38.1^{\circ}\text{C}$ . In the urine albumin and plenty of red blood cells. Was again admitted on account of a new attack which set in a fortnight previously.

Admitted on Sep. 9. Affected general condition. Jaundiced. Temperature  $38.8^{\circ}\text{C}$ . Direct and indirect tenderness, most pronounced over the region of the gall bladder. Albumin in the urine. — Oct. 1. Meulengracht 55. —



*Cholecystectomy* and *choledocholithotomy*. Narcosis. Gall bladder of normal size and with thick walls. Considerable acute inflammation round the normal biliary ducts. From the common duct 5 spoons of a thick mass were removed. *Prep.*: strongly inflamed gall bladder with partly ulcerated mucous membrane and markedly flushed wall. It contained 2 stones and purulent, not bile-coloured liquid. — Oct. 5. After the operation the patient has been very weak, with recurrent vomitings. The quantities of urine decreased. — Oct. 6. Rest nitrogen 180. — Oct. 7. Died.

Autopsy: acute glomerulonephritis. Field of operation normal.

One patient died from heart and vessel disease.

10) 2118/1928. Woman, aged 74. Mild attacks of biliary colic for 30 years. Latest attack 4 days prior to admittance.

Admitted Aug. 9. Good general condition. Jaundiced. Temperature 37.9° C. Tenderness over the region of the gall bladder. — Aug. 13. X-ray examination: no contrast filling of the gall bladder. At the site of the gall bladder 4 stones are visible, one of which probably lies in the common duct. — Aug. 14. The jaundice increases. Skin bleedings. — Aug. 15. *Cholecystectomy* and *choledocholithotomy by way of the cystic duct*. Between the gall bladder and the duodenum an abscess is found, containing a small gall stone. The gall bladder thick and shrivelled, containing white bile and 3 stones. The common duct strongly dilated. At Vater's papilla a stone which was removed by way of the cystic duct. — Aug. 26. Thrombosis in the right leg. — Sep. 3. Sudden death.

Autopsy: chronic myocarditis; arteriosclerosis. In the common bile duct a pea-sized stone was found, which did not cause stenosis of the passage.

One patient died from complication after blood transfusion.

11) 2713/1930. Man, aged 40. Several attacks for 5 years. Attack the day before admittance.

Admitted on Sep. 30. Affected. Jaundiced. Temperature 38.6° C. Tenderness and moderate rigidity in the abdomen above the umbilical plane. — Oct. 10. *Cholecystectomy* and *choledocholithotomy*. The gall bladder revealed little pronounced changes. The common duct was finger-thick, containing black bile (no bacteria in direct preparation). 11 pea-sized stones collected from the neighbourhood of Vater's papilla. *Prep.*: fibrous cholecystitis (pathological diagnosis). — Oct. 11. Sudden death after blood transfusion from donor of the same blood group.

Autopsy: Multiple thromboses in the cerebral artery; hyperplasia of the spleen and the medulla of the femur; infarction of the kidney. Field of operation normal.

In this case, either the determination of blood group was erroneous, or else the patient presented an abnormal reaction to foreign blood.

One patient died from acute pancreatitis.

12) 2060/1929. Woman, aged 64. First attack, setting in one week prior to admittance. Jaundiced 4 days before admittance.

Admitted on Aug. 13. Good general condition. Markedly jaundiced. Temperature  $37.8^{\circ}\text{C}$ . Tenderness over the region of the gall bladder. — Aug. 16. *Cholecystectomy with exploration and drainage of the common duct* by way of the cystic duct. The gall bladder was shrivelled; an abscess between the gall bladder and the liver. An obstacle was felt in the papillary portion of the common duct. Gradually, the probe passed into the duodenum and it seemed as if a stone had been conveyed into the intestine. *Prep.*: in the gall bladder thick bile and stones. Aug. 19. *Blood transfusion*. — Aug. 21. The patient is strongly affected, with poor pulse, peripheral cyanosis, dyspnea. Temperature around  $39^{\circ}\text{C}$ . Abundant flow of bile from the wound. *Blood transfusion*. — Aug. 23. Died.

Autopsy: acute hemorrhagic pancreatitis; gall stone in the pancreatic duct; bronchopneumoniae.

No doubt the stone found in the pancreatic duct had been accidentally brought there during the operation and had later on caused the acute pancreatitis.

The two remaining patients died from cholangitis.

13) 782/1932. Man, aged 51. 2 years previously treated for acute cholecystitis; had at that date had 5 attacks in 2 years. After the discharge from the hospital repeated attacks.

Admitted on March 15. Affected general condition. Frequent attacks. Temperature  $38.8^{\circ}\text{C}$ . Jaundiced. Intense tenderness over and medial of the region of the gall bladder. Immediate *cholecystectomy and choledocholithotomy by way of the cystic duct*. Local anesthesia; narcosis. The gall bladder small, hyperemic, thickened, containing greyish green bile (in direct preparation rods and cocci) and black particles of gravel. The cystic duct almost a little finger in width, was opened close to the common duct. In the hepatic duct a yellowish brown bile with clots of pus. Pea-sized fragments of a large papilla stone were removed. The liver was of a greyish colour and swollen. — Drainage tube in the cystic duct. — The day after the operation complete anuria. Died 5 days later.

Autopsy: chronic cholangitis and stone in common duct; cholangitic cirrhosis of the liver.

In this case, dextrose should have been administered intravenously both before and after the operation (which is also noted in the hospital diary). The changes found at the operation and later on in the post-mortem examination were so grave, however, that in all probability no measures could have saved the patient.

14) 2735/1933. Woman, aged 55. Had had 3 attacks in 7 years. Latest attack 3 days prior to admittance.

Admitted on Nov. 16. Pronounced jaundice. Temperature 39.3° C. Immediately after the admittance *cholecystectomy*, *choledocholithotomy* and *duodenorrhaphy*. Local anesthesia and mild narcosis. Shrivelled, solid liver. The gall bladder very thick, small. Between the gall bladder and the liver an abscess. During the operation the duodenum was injured and was sutured. Plenty of stones in the dilated common duct which was filled with pus. Pre p.: shrivelled gall bladder, the size of a forefinger, with both acute and chronic changes in the wall. — After the operation, subcutaneous and intravenous administration of plenty of invertose. The condition deteriorated, however, on Nov. 17 and the pulse was poor. — Nov. 23. Abundant vomitings the last days. Duodenal fistula. — Nov. 27. Still frequent vomitings. *Jejunostomy*. — Nov. 21. Everything the patient drinks, flows out through the duodenal fistula. Dec. 1. *Duodenorrhaphy*, *choledochorrhaphy* and *gastroenterostomy*; *blood transfusion*. Dec. 2. Died.

Autopsy: Hepatitis and cholangitis; recent gastric ulcer; bronchopneumoniae.

In this case, the duodenal lesion at operation no doubt contributed to the lethal issue.

The material is given in table 40. The mortality was lower among the cases which had no fever than among those in which fever was present. Out of the cases without fever, 25 had had no, or only mild, symptoms of stone in the common bile duct. None of these patients died. 3 patients, on the other hand, died among the 20 presenting symptoms of common duct stone.

Fever was present in 57 cases. Among 35 of these cases, in which no, or only mild, symptoms of common duct stone had been present, 5 died. In 15 out of the 35 cases the fever was probably mostly caused by co-existent acute cholecystitis, and in the remaining cases by acute pancreatitis or infection of the biliary ducts. 22 cases had symptoms both of common duct hindrance and of fever. No less than 6 out of these patients died.

In the total material 25 cases were present which in addition to common duct stone also had acute cholecystitis. In 6 of these, no clinical symptoms of common duct stone were present. 9 patients had mild jaundice and the remaining 10 symptoms of common duct hindrance. 4 out of the 25 patients died (deaths Nos. 1, 2, 9, and 12): one from pulmonary complication, one from disease of the kidneys, one from acute pancreatitis, and one from peritonitis developed from the cholecystitis.

Our material is small and the conclusions to be drawn from it as regards the risk involved in operation in the different groups into which the material was divided, therefore are rather indefinite. To judge from our material, the risk of operation for common duct stone is inconsiderable in the cases in which the stone gave few, or no, symptoms and in which the patient did not have fever. (No deaths among 25 cases.) The death-risk is greater in the cases in which the patient has few or slight symptoms of common duct stone and contemporaneously fever (5 deaths among 35 cases). The mortality is in these cases to a comparatively large extent determined by complications from gall bladder and pancreas. In the cases, finally, in which symptoms of common duct hindrance are present, the relative number of deaths is smaller among those who had no fever than among those who had fever (3 deaths among 20 cases, respectively 6 deaths among 22 cases). The differences in the figures for the postoperative mortality between the different groups to be obtained on the basis of our material, however, are statistically neither significant nor probable. The material is small and in consequence it might well be imagined that, since differences of this kind seem *a priori* probable, larger materials might yield a significant difference in the death-risk after operation between the different groups of cases and between cases without fever and with fever.

### **Re-examination of the cases operated on.**

In numerous papers the after-results of operative treatment of gall stone disease have been discussed. We have mentioned above (p. 169) that the frequency of relapse after cholecystostomy has been considered to be comparatively high but that, on the other hand, investigations exist indicating that the risk of relapse following cholecystostomy is not too great. Our material of cholecystostomies is small: it only comprises 10 cases, 5 of which died after the operation. Of the remaining 5 patients, 3 were operated on after the year 1930 and have therefore not been re-examined. Two patients were operated on in the years 1922—1930. Of these, one died 5 years after the treatment in the hospital from another disease, and one was later subjected to operation (cholecystectomy).

In the following we shall only discuss the re-examinations in the literature and in our own material which relate to cases of chole-



cystectomy. The early compilations in the literature generally deal with fairly small materials and refer to indications and general technique which are not wholly comparable to those adopted in more recent years. We have therefore restricted the survey of the literature to the time after 1920.

To a certain extent all the cases operated on, which are included in the materials presented in the literature, are discussed without regard being paid to the different forms of the disease which were treated. In the majority of the compilations, no data are given as to the distribution of the material on different age groups and sexes. In the materials from more recent years, particularly those published by American authors, cases of non-calculous cholecystitis are included to a comparatively large extent. In many re-examinations, further, a comparatively small part of the treated patients could be traced. We have pointed out above (p. 81) that we have cause for expecting that such selected materials will comprise a large part of the patients who have died or who have subsequently been operated on for their disease and that, consequently, it might be expected that the figures obtained on the basis of such materials will show a higher tendency to relapse than actually is present. Finally, the time of observation is fairly short in some materials, at least for part of the patients. Such materials may be expected to yield figures for the tendency to relapse which are lower than what corresponds to the actual state of things.

In order to avoid a wearisome repetition we have brought together the results of the more important re-examinations in table 41. The table includes, so far as possible, only cases of cholecystectomy and only the result for the total materials. The cases in which the patient has had no discomforts from his disease, were denoted as free from symptoms. By mild symptoms it is implied that the patient has had isolated attacks or other discomforts which have not, however, encroached upon the patient's capacity for work. By severe symptoms it is denoted that the patients have had recurrent attacks which have invalidated them or later on made an operation necessary. To this group we have also referred the patients who subsequently died from their disease. In the cases in which the authors in question have stated that a certain number of patients were healthy and that others had had more or less severe discomforts, the cases belonging to the latter group were accounted for under the heading of severe symptoms.

Table 41. *Re-examination of cases operated on. Data from the literature.*

| A u t h o r                           | Number<br>Re-ex-<br>amined<br>of these<br>cases<br>N | Time of<br>observation | Free from<br>symptoms |        | Mild<br>symptoms |        | Severe<br>symptoms |        |
|---------------------------------------|------------------------------------------------------|------------------------|-----------------------|--------|------------------|--------|--------------------|--------|
|                                       |                                                      |                        | Number                | % of n | Number           | % of n | Number             | % of n |
| ROHDE 1920 .....                      | 272                                                  | 107                    | 86                    | 80.4   | —                | —      | 21                 | 19.6   |
| LIEK 1921 .....                       | 93                                                   | 75                     | 51                    | 68.0   | —                | —      | 24                 | 32.0   |
| HINZ 1921 .....                       | 89                                                   | 58                     | 33                    | 57.9   | 15               | 26.3   | 10                 | 17.5   |
| BRENTANO 1923 .....                   | 243                                                  | 120                    | 71                    | 59.2   | 23               | 19.2   | 26                 | 21.7   |
| GRAMÉN 1923 .....                     | 172                                                  | 77                     | 59                    | 76.6   | 16               | 20.8   | 2                  | 2.6    |
| SIMON and SCHLEGEL 1923 .....         | 223                                                  | 140                    | 124                   | 88.6   | —                | —      | 16                 | 11.4   |
| KROGIUS 1924 .....                    | 142                                                  | 103                    | 71                    | 68.9   | 26               | 25.2   | 6                  | 5.8    |
| SEULBERGER 1925 .....                 | 304                                                  | 217                    | 110                   | 50.7   | 70               | 32.3   | 37                 | 17.1   |
| CAVE 1926 .....                       | 440                                                  | 209                    | 182                   | 87.1   | —                | —      | 27                 | 12.9   |
| HITZROT and CORNELL 1926 .....        | 363                                                  | 347                    | 203                   | 58.5   | 112              | 32.3   | 32                 | 9.2    |
| FLÖRCKEN 1926 .....                   | —                                                    | 273                    | 206                   | 75.5   | 41               | 15.0   | 26                 | 9.5    |
| DAHL-IVERSEN 1927 .....               | —                                                    | 156                    | 126                   | 80.8   | 11               | 7.1    | 19                 | 12.1   |
| HUECK 1927 .....                      | 263                                                  | 135                    | 89                    | 65.8   | 20               | 14.9   | 26                 | 19.3   |
| DEAVER and BORTZ 1927 .....           | 385                                                  | 355                    | 289                   | 81.4   | 49               | 13.8   | 17                 | 4.8    |
| LÜTZOW-HOLM 1928 .....                | 142                                                  | 119                    | 73                    | 61.3   | 30               | 25.2   | 16                 | 13.5   |
| DAVIS 1928 .....                      | 154                                                  | 144                    | 100                   | 69.4   | 38               | 26.4   | 6                  | 4.2    |
| PETERMANN 1928 .....                  | —                                                    | 540                    | 459                   | 85.0   | 54               | 10.0   | 27                 | 5.0    |
| MICHELSON 1929 .....                  | 656                                                  | 375                    | 261                   | 69.6   | 92               | 24.5   | 22                 | 5.9    |
| KMENT 1930 .....                      | 370                                                  | 275                    | 208                   | 75.6   | 42               | 15.3   | 25                 | 9.1    |
| SANDERS 1930 .....                    | 462                                                  | 352                    | 296                   | 84.1   | 42               | 11.9   | 14                 | 4.0    |
| FOWLER 1933 .....                     | 916                                                  | 814                    | 705                   | 86.6   | 79               | 9.7    | 30                 | 3.7    |
| WALDEYER 1933 .....                   | —                                                    | 253                    | 158                   | 62.5   | 87               | 34.4   | 8                  | 3.2    |
| WILSON, LEHMAN and GOODWIN 1937 ..... | —                                                    | 308                    | 243                   | 78.9   | —                | —      | 65                 | 21.1   |

With a view to adding to the table we shall in the following pages give some pieces of information relating to conditions which could not be included in the table and which we have to know about in order to gauge the figures in a correct manner. We principally refer to data given by certain authors on the state of health in special groups of cases operated on (cases with acute cholecystitis, common duct stone, chronic calculous cholecystitis).

ROHDE had himself re-examined cases »jahrelang nach der Operation». In LIEK's material, a number of cases of cholecystostomy are included. HINZ divides his material into three groups. Of the 29 cases operated on in a chronic stage (part of those had stone in the common duct), 16 were free from symptoms, 6 had mild, and 7 severe, symptoms. Of the 21 patients who were operated on for acute cholecystitis, 14 were healthy, 6 had mild, and 7 severe, discomforts. Of the 8 cases, finally, which had been operated on for acute cholecystitis and stone in the common bile duct, 3 were healthy, 3 had mild, and 2 severe, discomforts. In SIMON and SCHLEGEL's material of 140 re-examined cases, choledochotomy was performed in 46 cases. Out of the 16 patients who had more or less severe discomforts after the operation, choledochotomy was performed in 11 cases. HUECK in his material which includes 38 cases in which no stone was found, had 59 cases which had been operated on for acute cholecystitis. Of these 35 were healthy, 12 had diffuse discomforts and 12 had attacks of pain. He further grouped his cases with regard to the duration of the anamnesis. Of 50 cases which at the time of operation had had one attack, or attacks during a fairly short period, 64 per cent were healthy, 18 per cent had diffuse discomforts, and 18 per cent had attacks of pain. Of 85 cases which had had the disease over a prolonged period, the corresponding percentage figures were 56, 21, and 23. The material was further grouped according to the patient's age at the time of operation. Out of 68 patients who were under the age of 40, 59 per cent were healthy, 19 per cent had diffuse discomforts and 22 per cent had attacks of pain. The corresponding figures for the 67 patients who were over 40, were 59, 20, and 21. In KMENT's material are included 13 cases operated on during the acute attack. 11 of them were healthy and 2 were improved. Of the 262 cases operated on during the stage of interval, 78 per cent were healthy.

Some writers have only examined certain groups of cases (these investigations are not entered in the table). SMITH (1933) re-examined cases of acute cholecystitis. The time of observation was 2 months up to several years. Of 71 cases operated on during the acute stage, 83 per cent were healthy or improved, 13 per cent had more or less marked discomforts, and 4 per cent had cicatricial hernia. Out of 68 cases operated on during the interval, 90 per cent were healthy or almost healthy, while the other patients had more or less severe discomforts. BRANCH and ZOLLINGER (1936) also re-examined 152 cases of acute cholecystitis which had been kept under observation for at least 2 years. 110 (i. e. 72 per cent) of them were healthy. LIEDBERG (1937) re-examined 260 out of 262 patients cholecystectomized for acute cholecy-

stitis. 77 among these were observed between 2—5 years. Of these 55 were healthy, 10 had fairly mild symptoms and 12 had more severe symptoms. The remaining 183 cases had been observed between 5 and 10 years. Of these, 125 were healthy, 28 had fairly mild symptoms and 30 more severe discomforts. The material is further analysed with regard to the patient's age at the time of operation, the length of the anamnesis and the stage at which the operation was performed (during attack or interval), and finally with regard to the more or less severe grade of the cholecystitis. The investigation showed that these factors were not important to the result of the treatment. Of the total material, 180 (i. e. 69,2 per cent) were healthy after operation. 38 (i. e. 14,6 per cent) had fairly mild discomforts and 42 (i. e. 16,2 per cent) had more severe discomforts. Of the latter cases, 2 had died from gall stone disease and one case had later on been operated on.

FINSTERER (1935) had re-examined 303 cases, which were kept under observation between 3 and 20 years. 70 of these had been operated on during the acute attack. Of these, 64 (i. e. 91,4 per cent) were quite healthy, 4 had mild discomforts and the remaining cases had severe symptoms. 178 patients had been operated on in the interval. 142 (i. e. 79,8 per cent) were healthy whereas 12 had fairly mild symptoms and 24 more severe symptoms. Out of 13 cases, in which common duct stone had been removed by choledochotomy, 5 were healthy. Finally, 40 were healthy out of 42 cases in which choledochoduodenostomy had been performed.

BERNHARD (1935) re-examined 687 out of 901 cases, in which choledochotomy had been performed. 389 cases were quite healthy (i. e. 56,6 per cent). The remaining cases had more or less severe symptoms.

In summing up we may state that the material of figures presented shows that between 50 and 90 per cent of the cholecystectomized patients were healthy, or almost healthy. In the case of materials of patients operated on which are only accounted for in their entirety, we should maybe not pay too much attention to the percentage of healthy individuals. It might be imagined that the materials are not comparable: in one material may be included a comparatively large number of early and mild cases, in another material it may be the other way round. Re-examinations of specific groups of cases operated on are comparatively sparse. They show, however, that no significant difference seems to be present between the results of cholecystectomy in more acute cases as compared to more chronic cases.

#### **The author's material.**

In the years 1922—1930, cholecystectomy for gall stone disease was performed in 380 cases. Of these, 32 died relative to the operation. To the remaining 348 patients a questionnaire was sent si-



milar to the one given on p. 83. Part of the earlier treated patients were re-examined during the year 1931, and the rest during the years 1935—1936; in 1937 certain supplementary re-examinations were made. Data were obtained on 333 patients, i. e. 95,7 per cent. It was not possible to receive information on 15 patients for the reason that they were unknown to the register offices in question; consequently, we could not get into contact with them. In the treatment of the material no regard was paid to these cases which were excluded at random from the re-examination and whose number is moreover small. It does not seem probable that the result of the re-examination would have been essentially modified if information had been received on these cases.

The time of observation in the material was between 3 and 15 years, on an average 7,2 years. In 3 cases the time of observation was 3 years, in 38 cases 4 years, in 30 cases 5 years, and in the remaining cases at least 6 years. An examination of the same type as the one described on p. 84 for the patients not operated on shows that 75 patients have had attacks of pain after the operation. In 37 of these cases, it is only stated that the patient has had attacks. In 38 cases, information is given as to the time of the attack. In 14 out of these 38 cases the attack appeared within the first year of the operation, in 4 cases within 1—2 years of the operation, in 5 cases within 2—3 years of the operation, in 7 cases within 3—4 years of the operation and in the remaining 8 cases, 5—7 within 7 years after the operation. With a time of observation of 4 years we were thus likely to obtain data on  $\frac{3}{4}$  of the relapses whereas the other relapses only appeared at a later date. When we are concerned with cases operated on, however, we are to a certain extent faced with a different situation from the one applying to cases not operated on. The number of relapses in the material is comparatively small, and the modification of the figure for the frequency of relapse we might obtain with a longer period of observation accordingly should not be very great. In our material, the time of observation is in most cases comparatively long and we consequently may expect that the figures for the frequency of relapse to be obtained on the basis of the material, do not differ very much from those representing the actual state of things.

With regard to the state of health after operation, the material was divided into three groups in the same manner as was done

with the cases not operated on. As clinically healthy were classified the patients who after the operation had been quite healthy or at most had had an isolated and not too severe attack of biliary colic. As mild symptoms were classified isolated and fairly mild attacks which did not encroach upon the patient's general state of health or capacity for work. In the group of severe symptoms are included recurrent attacks of biliary colic, or other symptoms of the gall stone disease which have resulted in the patients' health and capacity for work becoming reduced or lost. To this group of cases were further referred those who had later on been operated on for their disease (10 patients) and those who had subsequently died from the disease (2 patients).

Of the 333 patients, 31 had died after the stay in the hospital. 2 of these had died from gall stone disease:

2381/1927. Man, aged 65. In 1927 *cholecystectomy* and *choledocholithotomy*. In the common duct plenty of stones. Was taken ill 2 months after the discharge from the hospital with attacks of pain, chills, and tenderness in the region of the gall bladder. Since that time recurrent such attacks.

Was again admitted on April 13, 1928. Was markedly affected generally, and slightly jaundiced. Temperature  $39.8^{\circ}\text{C}$ . In the region of the gall bladder a solid, tender resistance. Died on April 14 during a rise of temperature up to  $41.6^{\circ}\text{C}$ . No autopsy.

To judge from the clinical picture the patient had a grave acute cholangitis.

1037/1927. Woman, aged 69. In 1927 *cholecystectomy* and *choledocholithotomy*. A stone, the size of a dove's egg, and a number of smaller stones were found in the common bile duct, which also contained thick pus. After the discharge from the hospital recurrent severe attacks with chills.

Was again admitted to the hospital in 1931. Temperature  $39.3^{\circ}\text{C}$ . Jaundice. Died on Nov. 18.

Autopsy: Croupous pneumonia; interstitial hepatitis; choledocholithiasis. In the common bile duct a plum-sized stone was found.

The remaining 29 patients had died from other diseases:

|                               |    |       |
|-------------------------------|----|-------|
| heart and vessel disease..... | 17 | cases |
| pulmonary disease .....       | 5  | »     |
| cancer in other organs .....  | 5  | »     |
| other disease .....           | 2  | »     |

The two abovementioned patients who died from gall stone disease after the discharge from the hospital, were included in the material and are reported on in the group of patients having had severe symptoms from the disease. The remaining 29 cases who

died from a disease other than gall stone disease, on the other hand, were not included, as reliable data could not be obtained as to the state of health in the majority of the cases.

The material was divided into different groups with regard to the time during which the patient was ill. In the case of 7 patients, no information is given as to the time during which they were ill before they were operated on. Of these 7 cases, which for this reason were not included in the analysis of the material, 4 were clinically healthy, one had mild discomforts, and 2 had severe symptoms. The modifications in the figures for the total material which are obtained if these cases are included, are comparatively slight.

Table 42. *Re-examination of patients operated on (exclusive of those who died from disease other than gall stone disease).*

| Number of attacks at<br>time of operation | Number<br>of cases,<br>N | Clinically<br>healthy |        | Mild<br>symptoms |        | Severe<br>symptoms <sup>1)</sup> |        |
|-------------------------------------------|--------------------------|-----------------------|--------|------------------|--------|----------------------------------|--------|
|                                           |                          | Number                | % of N | Number           | % of N | Number                           | % of N |
| <i>Non-complicated cases</i>              |                          |                       |        |                  |        |                                  |        |
| at most 2 attacks .....                   | 18                       | 17                    | 94,4   | 1                | 5,6    | —                                | —      |
| more than 2 attacks ...                   | 117                      | 89                    | 76,1   | 21               | 17,9   | 7                                | 6,0    |
| diff. %                                   |                          | +18,3 ± 6,7           |        |                  |        |                                  |        |
| <i>Cholelithiasis</i>                     |                          |                       |        |                  |        |                                  |        |
| at most 2 attacks .....                   | 11                       | 11                    | 100,0  | —                | —      | —                                | —      |
| more than 2 attacks ...                   | 74                       | 54                    | 73,0   | 16               | 21,6   | 4                                | 5,4    |
| diff. %                                   |                          | +27,0 ± 5,2           |        |                  |        |                                  |        |
| <i>Chronic cholecystitis</i>              |                          |                       |        |                  |        |                                  |        |
| at most 2 attacks .....                   | 7                        | 6                     | 85,7   | 1                | 14,3   | —                                | —      |
| more than 2 attacks ...                   | 43                       | 35                    | 81,4   | 5                | 11,6   | 3                                | 7,0    |
| diff. %                                   |                          | +4,3 ± 14,5           |        |                  |        |                                  |        |
| <i>Acute cholecystitis</i>                |                          |                       |        |                  |        |                                  |        |
| at most 2 attacks .....                   | 35                       | 34                    | 97,1   | —                | —      | 1                                | 2,9    |
| more than 2 attacks ...                   | 79                       | 58                    | 73,4   | 13               | 16,5   | 8                                | 10,1   |
| diff. %                                   |                          | +23,7 ± 5,7           |        |                  |        |                                  |        |
| <i>Common duct stone</i>                  |                          |                       |        |                  |        |                                  |        |
| at most 2 attacks .....                   | 13                       | 7                     | 53,8   | 4                | 30,8   | 2                                | 15,4   |
| more than 2 attacks ...                   | 35                       | 27                    | 77,1   | 3                | 8,6    | 5                                | 14,3   |
| diff. %                                   |                          | -23,3 ± 15,5          |        |                  |        |                                  |        |
| <i>Total material</i>                     |                          |                       |        |                  |        |                                  |        |
| at most 2 attacks .....                   | 66                       | 58                    | 87,9   | 5                | 7,6    | 3                                | 4,5    |
| more than 2 attacks ...                   | 231                      | 174                   | 75,3   | 37               | 16,0   | 20                               | 8,7    |
| diff. %                                   |                          | +12,6 ± 4,9           |        |                  |        |                                  |        |

<sup>1)</sup> inclusive of those re-operated on and deaths from gall stone disease.

*The total material.*

297 cases are consequently included in the following analysis. The total material is given in table 42. Out of the 297 cases, 232, i. e. 78,2 per cent, were quite healthy. 42 patients, i. e. 14,1 per cent, had mild discomforts and 23 patients, i. e. 7,7 per cent, had severe discomforts. Of the last-mentioned 23 patients, 2 had subsequently died from their disease (see above p. 191). 10 patients had been re-operated on for their disease. These are accounted for below, p. 199.

Of the 297 patients, 43 were men. Among these, 36 i. e. 83,7 per cent, were quite healthy. 254 patients were women. Among these, 196 were clinically healthy, i. e. 77,2 per cent. No statistical difference is present between the percentage of clinically healthy men and the percentage of clinically healthy women in our material (diff. =  $6,5 \pm 6,2$ ). In the subsequent analysis of the material the two sexes have been brought together, as otherwise the groups in which the material is divided, would be too small and as no difference could be demonstrated in the percentage of clinically healthy subjects between men and women in the material in its entirety.

We have above, in chapter V, shown that in the case of patients not operated on the risk of relapse was considerably smaller for those who had had only 2 attacks than for those who had had several attacks. In this chapter it was also pointed out that in the clinic in Uppsala it was for this reason avoided, if possible, to operate on those who had had one or two attacks. In the material of cases operated on which was re-examined, that is to say the material for the years 1922—1930 (297 cases), there are 66 patients who had at most 2 attacks before the operation. In a way, this figure does not seem to indicate that operations are actually avoided in such cases. The fact is, however, that the majority of the patients who have had at most 2 attacks and who were operated on, presented acute cholecystitis (35 out of 114 cases, i. e. 30,7 per cent). In the case of patients with acute cholecystitis we have now and then cause for operating even if the patient has only had his disease a short time. In gauging the indications for operation in these cases, we have to pay more regard to the actual death-risk run by the patient than the potential risk of relapse. Of the remaining cases, 31 patients out of 183 were operated on who had had at most 2 attacks, i. e. 16,9 per cent. It should be noticed, however, that it



is especially after the year 1930 that more definite attempts have been made to avoid operation in the cases in which the patients have had at most 2 attacks.

Of the cases operated on and re-examined, 66 had had at most 2 attacks. Among these, 58 (i. e. 87,9 per cent) were clinically healthy. Of the remaining 231 cases who had had more than 2 attacks, 174 (i. e. 75,3 per cent) were clinically healthy. The difference is statistically probable (diff. =  $12,6 \pm 4,9$ ). The material consequently indicates that the state of health after cholecystectomy is somewhat better among those who were operated on for their first or second attacks, than among those who had had several attacks.

In order further to analyse the part of the material comprising patients who had had more than 2 attacks before the operation, we have divided this part of the material into two groups. One comprises the patients who had been ill during a time of at most 2 years. Among the 93 cases in this group, 73 (i. e. 78,5 per cent) were clinically healthy. The second group comprises those who had had attacks over a longer period than 2 years. Of the 138 cases, 101 were clinically healthy (i. e. 73,2 per cent). The difference between these two groups is not statistically probable (diff. =  $5,3 \pm 5,7$ ). The chance of recovery after operation consequently in our material was equally great for those who had had attacks over fairly short periods as compared to those who had had attacks over a prolonged period, provided that the patient had had more than 2 attacks (see table 43).

If we further examine whether the chance of recovery after operation is dependent on the age at which the patient was operated on,

Table 43. *Re-examination of patients operated on. Distribution according to duration of disease.*

| Duration of disease                           | Number of cases, N | Clinically healthy |        | Mild symptoms |        | Severe symptoms <sup>1)</sup> |        |
|-----------------------------------------------|--------------------|--------------------|--------|---------------|--------|-------------------------------|--------|
|                                               |                    | Number             | % of N | Number        | % of N | Number                        | % of N |
| At most 2 attacks .....                       | 66 <sup>2)</sup>   | 58                 | 87,9   | 5             | 7,6    | 3                             | 4,5    |
| More than 2 attacks during 2 years at most... | 93                 | 73                 | 78,5   | 16            | 17,2   | 4                             | 4,3    |
| More than 2 attacks during more than 2 years  | 138                | 101                | 73,2   | 21            | 15,2   | 16                            | 11,6   |

<sup>1)</sup> inclusive of those later operated on and deaths from gall stone disease.

we find that our material does not show any difference on this point: Out of 180 patients who were under the age of 50 at the time of operation, 137 were clinically healthy at the time of re-examination (i. e. 76,1 per cent), and of 117, who were over the age of 50 at the time of operation, 95 were clinically healthy (i. e. 81,2 per cent).

In the continued analysis the material has been divided with regard to the form of the disease for which the patient was operated on. The grouping was made in the same way as in the analysis of the post-operative mortality (see p. 101).

*The non-complicated cases.*

Of the 135 cases, 106 (i. e. 78,5 per cent) were clinically healthy, 22 (i. e. 16,3 per cent) had mild discomforts, and 7 (i. e. 5,2 per cent) had severe discomforts. Of the latter, 4 had later been operated on for their disease.

If we divide the material into one group comprising those who had had at most 2 attacks, and into another group comprising those who had had more than 2 attacks, we find that of the cases in the former group, 94,4 per cent were clinically healthy and of the cases in the latter group, 76,1 per cent were clinically healthy. The difference is statistically probable (diff. =  $18,3 \pm 6,7$ ). The material evidently seems to indicate that the chance of recovery after operation among the non-complicated cases is better for those who have had at most 2 attacks than for those who have had several attacks (see table 42).

Among the non-complicated cases are included both such cases in which the gall bladder presented no, or only little pronounced, changes (cholelithiasis in the proper sense of the term) and cases in which the gall bladder showed inflammatory changes (chronic cholecystitis). If we examine the results of treatment for these groups taken separately, we find as follows.

Of the 85 cases of cholelithiasis, 65 (i. e. 76,5 per cent) were clinically healthy. Of those who had had at most 2 attacks, all were healthy, and of those who had had more than 2 attacks, 73,0 per cent were clinically healthy. The difference is statistically significant (diff. =  $27,0 \pm 5,2$ ). We consequently find that the prognosis among the cases of cholelithiasis was more favourable for those who had had at most 2 attacks than for those who had had more than 2 attacks.

Of the 50 cases with chronic cholecystitis, 41 (i. e. 82 per cent) were clinically healthy. Among those who had had at most 2 attacks, 6 out of 7 cases were clinically healthy, and among those who had had more than 2 attacks, 35 out of 43 were clinically healthy. The material for this group is too small to allow of any conclusions as to the prognosis for the different groups.

The result of the re-examination of the non-complicated cases accordingly is that the majority of those operated on were clinically healthy, and that, only in the cases which presented cholelithiasis in the proper sense of the term, a difference could be demonstrated in the tendency to relapse between those who had had at most 2 attacks and those who had had several attacks.

#### *Acute cholecystitis.*

Of the 114 cases, 92 (i. e. 80,7 per cent) were clinically healthy, 13 had mild symptoms, and 9 had severe symptoms. Of the latter 5 had subsequently been operated on for their disease (see table 42).

Among those who had had at most 2 attacks, 97,1 per cent were clinically healthy, among those who had had more than 2 attacks, 73,4 per cent were clinically healthy. The difference is statistically significant (diff. =  $23,7 \pm 5,7$ ). See table 42.

The chance of becoming clinically healthy after operation among those who were operated on for acute cholecystitis, in our material consequently was better for those who had had at most 2 attacks than for those who had had several attacks.

#### *Choledocholithiasis.*

Of the 48 patients, 34 were clinically healthy, 7 had mild symptoms, and 7 had severe symptoms. Of the latter, one had subsequently been operated on for his disease and 2 had died from the disease without having been operated on (see above p. 191). Of the 13 patients who had had at most 2 attacks, 7 were clinically healthy, and of the 35 patients who had had more than 2 attacks, 27 were clinically healthy. No statistically significant difference can be demonstrated between these two groups of cases (diff. =  $23,3 \pm 15,5$ ). It should be noticed, however, that the material referring to those who had had at most 2 attacks, is so small that no definite conclusions could be drawn (see table 42).

The re-examination of the different groups of cases has shown that the chance for a patient of becoming clinically healthy after an operation for gall stone disease is fairly independent of the form of the disease for which the patient was operated on. For the cases of cholelithiasis and for the cases of acute cholecystitis we have been able to show that the chance of recovery is better for those who have had at most 2 attacks than for those who have had more than 2 attacks.

As mentioned above, 78,2 per cent of the patients in the material were clinically healthy after operation. If to these patients we add those who have only had mild discomforts of their disease and whose capacity for work and general state of health have not been to a large extent reduced on account of the disease, we find that 92,3 per cent of all the patients have shown a satisfactory, or comparatively satisfactory, state of health after operation.

*Causes of discomforts after cholecystectomy.*

To some extent it falls beyond the scope of this investigation to try to analyse the causes underlying the fact that part of the patients operated on have continued symptoms of the disease. The literature on this subject is very extensive. To a certain extent, more or less well-grounded assumptions as to the causes of such discomforts have been propounded. The patients in our material were only re-examined by questionnaires. The possibilities of obtaining really reliable data on the causes of the after-symptoms are therefore comparatively small. To the divergent data given on various symptoms from the gastrointestinal tract naturally cannot be ascribed too great an importance, as such discomforts occur comparatively frequently even in patients who do not present gall stone disease.

The most important cause of symptoms, at least of severe symptoms, is without doubt *stone in the common bile duct*. As a rule it is considered that common duct stone is not formed in the common duct. ROVSING's theory that such stones are formed in the biliary ducts has hardly any supporters. If we start from the assumption that stones are not formed in the biliary ducts, we must suppose that the common duct stones which have been found in operations for relapse, were overlooked in the first operation. Experience from many quarters shows that common duct stone has in many cases not given typical symptoms and may even be present without giving any clinical symptoms at all. In recent years the demand



has more and more been put forward that the common bile duct ought to be explored at operation for gall stone disease.

An examination of the common bile duct may be made in varying manners. In our material the common duct was comparatively often examined in such a way that from the cystic duct a probe and gall spoon were introduced and attempts were made to find out whether the passage through the common duct was free and also to remove stones that might possibly be found in it. In addition to this, the passage through the common bile duct was checked up on by irrigation of the duct. These examinations of the common bile duct were carried out to a comparatively great extent. Of the 99 cases in which common duct stone was found at operation, stones could be removed by way of the cystic duct in 37 cases. In the remaining 62 cases choledochotomy was performed.

In the other 511 cases in which cholecystectomy was performed, the common duct was explored from the cystic duct in 218 cases, and by choledochotomy in 25 cases. In all, the common duct was consequently explored in 243 cases out of 511 (i. e. 47,5 per cent of the cases).

It has been objected that common duct stone might escape discovery in spite of the common bile duct being explored in the way mentioned above. In recent years, X-ray examinations of the common duct with contrast media (cholangiography) have been made relative to the operation in many quarters (Mirizzi, 1933, DESPLAS, MOULONGUET and MALGRAS, 1938, and others). In the Uppsala clinic, HULTÉN in 1937 began to make cholangiography relative to the operation. On the basis of such examinations it has been considered that common duct stone could be demonstrated in a larger number of cases than previously.

We might try to form an idea of the extent to which an overlooked common duct stone causes discomforts after operation for gall stone disease by examining the cases which were later on re-operated for their disease. In this way we naturally may only obtain a minimum figure for the frequency of common duct stones left behind at operation.

In our re-examined material 10 patients are included who were subsequently operated on for their disease. Of those, 9 had been operated on in the Academical Hospital.

1) 1922 B/280. Woman, aged 54. Had had several attacks over a period of 15 years. May 12. *Cholecystectomy* and *choledochotomy*. Small shrivelled

gall bladder containing pus. The common duct was strongly dilated and contained slightly turbid bile. Stone could not be found in the common duct. Discharged; recovered.

Re-admitted in 1925. Had been free from symptoms for one year, then had recurrent attacks attended by chills, pains and jaundice. Oct. 2, 1925. *Choledochotomy* and *dilatation of common duct stricture*. The common duct was strongly dilated with thick walls above a stricture which could be dilated by probes, however.

At re-examination in 1935, the patient stated that she had had numerous severe attacks of pain but no jaundice.

2) 1923, B/535. Woman aged 24. Had had 3 attacks in  $\frac{1}{2}$  year, not combined with jaundice. Was admitted for acute cholecystitis. Temperature  $39.1^{\circ}$  C. Mild jaundice. Sep. 24. *Cholecystectomy*. Inflamed gall bladder. Discharged; recovered. After the discharge she had attacks of pain in Nov. the same year, and in Feb., 1924.

Re-admitted on March 31, 1924. No jaundice. April 11. *Choledocholithotomy*. In the common bile duct a pea-sized stone was found. Has since been free from symptoms from the biliary ducts.

3) 1926/3029. Woman, aged 42. Recurrent attacks for 20 years. 2 years previously cholecystostomy had been performed in another hospital, after which a fistula remained. Dec. 3. *Cholecystectomy* and *probing of the common duct from the cystic duct*. No stones could be discovered in the common duct. After the discharge the patient has had repeated, severe attacks, but no jaundice.

Re-admitted in 1929. March 20. *Choledocholithotomy*. In the finger-wide common duct 2 pea-sized stones were found.

At the re-examination in 1935 the patient stated that she had had recurrent severe attacks attended by chills but not by jaundice.

4) 1927/707. Woman, aged 70. Recurrent attacks for 25 years. No jaundice. Admitted for acute cholecystitis with a temperature of  $39^{\circ}$  C. and mild jaundice. March 14. *Cholecystectomy*. No changes in the common duct could be palpated. Discharged; recovered.

In Nov. the same year a new attack with a temperature of  $39^{\circ}$  C. and jaundice. Nov. 13. *Choledocholithotomy*. Finger-wide common duct in which was found a stone the size of a red bean.

After the operation free from symptoms (re-examined in 1935).

5) 1928/627. Man, aged 58. Recurrent attacks over a period of 6 years. The attacks combined with jaundice. Admitted for acute cholecystitis. Feb. 27. *Cholecystectomy* for gangrenous cholecystitis. From the wound abundant flow of bile; on this account *choledocholithotomy* was performed by way of the cystic duct on April 1. In the common duct small stones were found. Discharged; recovered.

At the re-examination in 1936 the patient stated that he had been quite healthy after the last operation.

6) 1928/941. Woman, aged 66. Repeated attacks for 12 years. Sometimes jaundice. April 2. *Cholecystectomy*. Considerably shrivelled gall blad-

der. Admitted on April 13. Discharged; recovered. After the operation again attacks with pronounced jaundice.

Re-admitted on Sep. 1. Temperature 38° C. Jaundice. Sep. 7. *Chole-dochotomy*. The common duct was strongly dilated but contained no stone. The pancreatic caput was considerably thickened and hard. In the omentum fatty necroses. Discharged; recovered.

At the re-examination in 1935 the patient stated that she had been healthy after the operation.

7) 1928/1930. Woman, aged 28. Repeated attacks over a period of 10 years. Admitted on May 12. Mild jaundice. Temperature 37° C. May 14. *Cholecystectomy*. Numerous stones in the gall bladder and in the cystic duct. Discharged; recovered. After the discharge new attacks, but no jaundice.

Re-admitted July 17 after new attack. July 18. *Choledocholithotomy*. It was possible to remove a fragment of a faceted stone from the dilated common duct. Discharged; recovered.

At the re-examination in 1936 the patient stated that she had had a few attacks after the discharge from the hospital but on the whole had been comparatively healthy.

8) 1930/1922. Woman, aged 61. 2 attacks over a period of 1½ years and jaundice in connection with the attacks. Admitted on July 7. Temperature 38.5° C. Jaundice. July 18. *Cholecystectomy* and *choledocholithotomy*. From the finger-wide common duct 3 pea-sized stones were collected. Discharged; recovered. Subsequently free from symptoms over a time of 2 years but later on had again severe attacks, combined with jaundice.

Re-admitted Oct. 15, 1932. Marked tenderness over the gall bladder. Oct. 24. *Choledochotomy* and *resection of the duodenum*. A considerable amount of adhesions round the common duct. The duodenum was attached to the gall bladder bed and was injured. On account of this a transverse resection of the duodenum was made. The common duct was probed and no stone could be discovered in it. Oct. 30. The patient died.

Autopsy: *Choledocholithiasis*; hepatic abscess; acute pancreatitis; bronchopneumoniae. In the common duct was found one walnut-sized and one pea-sized stone.

9) 1930/1956. Woman, aged 48. Several attacks over a period of 3 years. Admitted on July 11 with symptoms of acute cholecystitis. July 16. *Cholecystectomy*. A number of small stones in the inflamed gall bladder. Discharged; recovered. After the discharge repeated attacks.

Re-admitted on Dec. 29, 1932. Temperature 38.5° C. Mild jaundice. Diastase value in the urine at least 1024. Jan. 2, 1933. *Choledochotomy*. The common duct was a forefinger in width but contained no stone. Discharged; recovered.

At the re-examination in 1936 the patient stated that she had been healthy after the last operation.

Of the 9 cases subsequently operated on, choledochotomy had been performed in one case (No. 1) at the first operation and no

stone had been found. At the re-operation a stricture was found which had caused the discomforts. In one case (No. 8) a stone had been removed from the common duct in the first operation, and stone was also present at the re-operation. In the remaining 7 cases the common duct had not been explored at the first operation. In 6 of these cases stone was found in the common duct at the re-operation.<sup>1)</sup>

The material consequently shows that in the majority of the cases which had to be operated on again, stone was present in the common bile duct, having caused discomforts, and further, that in all of these cases, with the exception of one, the common duct had not been explored at the first operation.

7 out of the 23 patients who presented severe discomforts, had also stone in the common bile duct. It is naturally possible that among the remaining cases the discomforts were to a certain extent also caused by common duct stone. Indication seems to be present for exploring the common bile duct in operation for gall stone disease to a larger extent than has previously been done. During the period covered by our material, common duct exploration was performed from the cystic duct or by choledochotomy. In recent years, as mentioned above, cholangiography is being adopted to a larger extent and it has by this means been possible, in a larger number of cases than before, to discover common duct stone which does not give clear clinical symptoms and consequently to lessen the risk of severe discomforts after the operation.

An evaluation of other causes of discomforts after operation, as for instance pancreatitis in different forms, adhesions, etc., is hardly possible on the basis of a material such as ours in which the patients were not re-examined in person. It is also difficult, without a close examination, to form an idea of the nature of the dyspeptic symptoms which are recorded by part of the patients. The frequency of such discomforts, however, was not high in our material. The patients who had been clinically healthy, had had no such discomforts, and among those who did not recover after operation, the attacks of pain dominated.

It might, on the other hand, be of interest to examine in what

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<sup>1)</sup> Further, in 5 of the cases operated on, common duct stone was found by autopsy.



percentage of the cases the patient, after the operation, was troubled by *hernia* in the scar. In our material, 10, i. e. 3,3 per cent of the patients recorded such hernias. It is natural that the frequency of hernia should be higher in a material which has been subjected to personal examinations than in a material in which the figures are based only on the data given by the patients themselves. It is, however, remarkable that the frequency of hernias in our material is unusually low as compared to that of other materials. PETERMANN found cicatricial hernias in 6 per cent of the cases, SANDERS in 8,5 per cent, CATTELL in 6 per cent, ROSENBAUM and WIESEN in 15,5 per cent, and LIEDBERG in 8,8 per cent. In the Uppsala clinic, a method for abdominal section, suggested by Professor NYSTRÖM, director of the clinic, has been employed and it seems very probable that this method involves a smaller risk of cicatricial hernia than other methods. The procedure is as follows.

The skin section is placed just below the right costal edge. The musculature is cut through in such a way that the external, internal and transverse musculature is divided in the longitudinal direction of the fibers. If possible, the rectus muscle is not divided; at most, a cut is made into it about one cm. from its lateral edge. Drainage is as a rule made after the operation, usually with two narrow tubes or with a »cigarette» and a tube. The drainage is conducted to the medial portion of the wound either by way of the partially split rectus muscle, the lateral edge of which is in that case sutured, or else immediately lateral of the non-split rectus muscle. It has not proved difficult to perform complicated biliary duct operations from the section described above and the wounds have as a rule healed primarily.

### Summary.

In the years 1922—1935, 620 patients were operated on for gall stone disease in the surgical department of the Academical Hospital in Uppsala. 57 of them had previously been treated for gall stone disease but not been operated on on that occasion.

261 patients had non-complicated gall stone disease. 5 of those died after the operation. Of the 261 cases, 175 belonged to the group of cholelithiasis, with one death. 86 patients, 4 of whom died, presented chronic cholecystitis.

257 patients were operated on for acute cholecystitis. 27 of those died after operation. In the early period, 1922—1931, 24 out of 171 patients died (i. e. 14,0 per cent); in the later period, 1932—1935, 3 out of 86 died, (i. e. 3,5 per cent). The difference in mortality is statistically significant. We have analysed the material in different manners in order to try to get an idea of the cause of this decreased mortality in recent years. Both the cases of acute cholecystitis not operated on and the cases operated on present no obvious changes in regard to age distribution, or to more or less severe grade of the disease. As regards the cases operated on, it has been shown that the patients have in recent years been operated on during a later stage of the disease, that is to say that the interval between the onset of the acute attack and the operation was longer. Such a displacement of the time at which the operation was performed has not involved an increased risk in the material, and probably caused, or contributed to, the decreased mortality. Other, unknown factors may naturally also have contributed to the latter.

102 patients were operated on for stone in the common bile duct. Of those, 14 died relative to the operation. The material was divided into three groups: a) the common duct stone gave no clinical symptoms, b) it gave indefinite clinical symptoms, c) it caused common duct obstruction. In each group the material was divided into cases with fever and cases without fever. The mortality figures are higher for the cases which presented fever than for those which did not present fever, and higher for those who had marked symptoms of common duct stone than for those who had no such symptoms.

The patients who were operated on in the years 1922—1930, 348 in number, have been re-examined. No data could be obtained on 15 patients. 31 patients had died after the stay in the hospital. In 7 cases no information is given as to the time of the first attack. Of the remaining 297 patients (inclusive of 2 patients who had died from gall stone disease), 232 (i. e. 78,2 per cent) were clinically healthy and 42 (i. e. 14,1 per cent) had mild discomforts. The other 23 patients had severe symptoms (i. e. 7,7 per cent). 10 out of the 23 patients had later on been operated on and 2 had died from gall stone disease.

On the basis of the material it has been shown that there is a statistical probability that the chance of recovery after operation is

greater for those who have had at most 2 attacks prior to the operation than for those who have had several attacks.

The material is further divided into different groups according to the form of disease from which the patient suffered. Of the non-complicated cases, 78,5 per cent were clinically healthy, of the cases with acute cholecystitis 80,7 per cent and of the 48 cases with common duct stone 34. In the non-complicated cases which presented cholelithiasis only, and in the cases with acute cholecystitis, the percentage of clinically healthy subjects was higher among those who had had at most 2 attacks at the time of operation than among those who had had several attacks.

9 patients had later on been operated on in the hospital and in 7 of these cases common duct stone had been found. Hernia was only present in 3,3 per cent. The method for abdominal section used in the clinic is described.

## CHAPTER 7.

### Gall Stone Disease from a Clinical Point of View.

In the foregoing chapters we have treated gall stone and gall stone disease from a demographic point of view. We have further dealt with the clinical cases, both those operated on and those not operated on, with regard to the immediate death-risk and the risk of relapse. In this chapter we shall try to weigh the different risks against one another and to obtain a picture of the clinical material as a whole, that is to say both of cases operated on and cases not operated on, and both with regard to death-risk and to risk of relapse. Obviously, an attempt to orientate on the general risk for groups of cases delimited in different ways can only give indications of a general type which may be more or less useful in deciding upon the treatment in an individual case. In that case, however, all the data on the case have to be utilized and factors of a special kind may be more important than the statistical generalizations, based on our material.

In the case of gall stone disease, we should formulate the problems in this way: What is the risk involved in an operation, and what is the risk run by the patient if he is not operated on? (By risk we refer in this connection to a) the risk of dying, b) the risk of having recurrent symptoms of the disease.) If the cases were quite similar, this simple formulation of the problem would be exhaustive. Unfortunately, the situation is not as simple as all that. The cases run a different risk, no matter if they are operated on or not, owing to the fact that the disease may vary in character. The characteristics which may vary, are three:

- 1) the grade of the infection,
- 2) the localization of the stone,
- 3) the age of the patient.



The questions formulated above ought to be repeated for all these three factors. This is difficult because the material is not sufficiently large to allow of a division into too many subgroups, and also because the line of demarcation between the different groups is not quite distinct.

**The risk of contracting different forms of gall stone disease.**

In some cases the disease is mainly characterized by attacks of pain which often cause very severe discomforts to the patient, it is true, but which are not directly threatening to life. In other cases the clinical picture is dominated by infection of the gall bladder. In many of these cases the infection is so intense that the disease involves a definite death-risk. In other cases, the clinical picture reveals symptoms caused by the gall stone being localized to the common bile duct, obstructing the passage. The factors causing the disease to appear now in one form, now in another, are not known. It is generally held that the more complicated cases, principally the cases in which the clinical picture is dominated by stone in the common bile duct, or grave infection of the gall bladder or biliary ducts, are those in which the disease is of a comparatively long standing. In other words, it has been maintained that the patient is exposed to a definite risk of developing a graver form of the disease if operation is avoided. On the basis of a clinical material we may try to get a certain idea of the actual state of the case on this point.

We have proceeded as follows. We have used the part of the material comprising the patients operated on. In these cases we may fairly accurately divide the material according to the form of the disease which has occurred, and distinguish between non-complicated cases and more complicated cases. We have divided the material into 4 groups:

- 1) Non-complicated cases of cholelithiasis, in which no infection of the gall bladder was present.
- 2) Cases with chronic cholecystitis.
- 3) Cases with acute cholecystitis.
- 4) Cases with common duct stone.

For each of these groups of cases, the average age at the time of the first attack was calculated, as also the average age at the time of operation. The differences between these two figures accordingly

Table 44. *Cases operated on for different forms of gall stone disease. Distribution according to average age at first attack and at operation.*

| Form of the gall stone disease | Number of cases | Average age at first attack | Average age at operation | Interval, years, between first attack and operation |
|--------------------------------|-----------------|-----------------------------|--------------------------|-----------------------------------------------------|
| Cholelithiasis .....           | 163             | 35,8                        | 40,7                     | 4,9 $\pm$ 0,6                                       |
| Chronic cholecystitis .....    | 86              | 40,8                        | 46,0                     | 5,2 $\pm$ 0,7                                       |
| Acute cholecystitis .....      | 253             | 44,4                        | 49,0                     | 4,6 $\pm$ 0,4                                       |
| Choledocholithiasis .....      | 102             | 47,2                        | 53,1                     | 5,9 $\pm$ 0,5                                       |

denote the average interval between the onset of the disease and the operation. Table 44 gives the result of this calculation. The table shows that the interval between the onset of the disease and the operation was the same for all the four groups of cases, about 5 years. The average age at which the patient was taken ill, on the other hand, as also the average age at the time of operation, show an increase from the mild cases to the more serious cases. The cases of cholelithiasis were taken ill at the average age of 35,8 years, the cases with chronic cholecystitis at the average age of 40,8, the cases with acute cholecystitis at the average age of 44,4, and the cases with common duct stone at the average age of 47,2. To judge from our material, the risk of being taken ill with a complicated form of the disease would be related to the fact that such forms appear at a more advanced age than in the case of a non-complicated form. Our material gives no support, on the other hand, to the assumption that the patients who were taken ill with a more complicated form of the disease, have been ill during a more prolonged period.

It might be objected that the figures given in the table are not reliable. It might be imagined that the non-complicated cases are all taken ill at about the same age and are all operated on at about the same age, so that the interval between the appearance of the disease and the operation is consequently the same for all patients. Matters may be different in regard to the complicated cases. The younger patients might be operated on a very short time after the beginning of the disease, while the elderly patients, and maybe the majority of the cases, are operated on when a considerably longer time has elapsed after the beginning of the disease. For the total material of complicated cases we then might obtain

Table 45. *Cases operated on for different forms of gall stone disease. Distribution according to average interval between beginning of disease and operation, for younger and older patients.*

|                             | Age at first attack | Average interval<br>between beginning<br>of disease and<br>operation |
|-----------------------------|---------------------|----------------------------------------------------------------------|
| Cholelithiasis .....        | < 35                | 6,5                                                                  |
|                             | > 35                | 3,7                                                                  |
| Chronic cholecystitis ..... | < 40                | 6,7                                                                  |
|                             | > 40                | 3,6                                                                  |
| Acute cholecystitis .....   | < 45                | 6,5                                                                  |
|                             | > 45                | 2,5                                                                  |
| Choledocholithiasis .....   | < 50                | 8,4                                                                  |
|                             | > 50                | 2,9                                                                  |

the same time interval between the beginning of the disease and the operation as for the non-complicated cases, in spite of the fact that, in the majority of the cases with complicated gall stone disease, the interval was longer than in the cases with non-complicated disease. In order to examine the actual state of the case, the material in each of the four abovementioned groups was divided into two parts, each part comprising about half of the material in each group. One half comprises the younger patients, the other the older patients. The age limit thus will approximately correspond to the average age for the appearance of the disease in each group. For both younger and older patients in each group of disease we have calculated the average interval between beginning of disease and operation. Table 45 shows that this interval in each group, i. e. both for the non-complicated and the complicated cases, is longer for the younger, than for the older, patients. The younger patients in each group were operated on between 6 and 7 years after the beginning of the disease, and the older patients between 3 and 4 years. No statistical difference is found in the intervals between beginning of disease and operation neither for the younger patients in the different groups, nor for the older patients. Under such circumstances the conclusion drawn above from our material may be correct, to the effect that *the risk of being taken ill with a complicated form of gall stone disease is greater the more advanced is the age at which the patient is taken ill*; on the other hand there is no evidence in support of the statement that the patients who

have been ill during a more prolonged period, would run a greater risk of being taken ill with a more complicated form of the disease.

In estimating the risk without operation, or with operation, for a patient suffering from gall stone disease, we must pay regard to the fact that the risk of dying from a disease is greater for older than for younger people, owing to a reduced resistance to morbid processes generally. In the case of gall stone disease, we moreover seem to have to reckon with the fact that the older the person is who is affected by the disease, the greater is the risk that the disease will appear in a more severe form.

#### **The risk of relapsing and of dying.**

If we want to establish what risks are incurred by persons suffering from gall stone disease, we must consider the varying characters of the cases. We have pointed out above that it is difficult to divide the material into circumscribed groups as regards the degree of the infection and the localization of the stone. In the case of patients operated on we are as a rule able to judge whether stone is present in the common bile duct or not. Further it is easier to estimate the degree of infection. It should be stated, however, that the clinical symptoms of a grave infection in gall bladder or biliary ducts may vary even if the infection is of the same type. Especially in elderly patients, the clinical symptoms of the infection are often milder than what actually corresponds to the degree of infection. In the case of patients not operated on we cannot as a rule decide whether stone is present in the common bile duct or not. We have repeatedly pointed out that stone may be present in the common duct without giving clinical symptoms. Further, the infection in the cases not operated on may be localized either to the gall bladder or to the biliary ducts, and nevertheless in both cases give about similar symptoms.

In trying to obtain an idea of the different risk factors in gall stone disease we had better adopt another ground of division for the material: we divide it into cases in which operation seems to be indicated owing to the serious nature of the cases, due either to infection or to obstruction in the common duct, or to both, and in cases in which the disease is milder in character, giving us the choice of operating or not operating.



*The severe cases.*

In the severe cases we are in fact only concerned with the actual death-risk. Only a secondary importance should reasonably be ascribed to the risk of relapse.

The severe cases of acute cholecystitis have been treated in different manners in our material. Some patients were admitted to the hospital in such a condition that operation could not have saved the patient (20 cases; they all died. Cf. p. 77—78). Other patients were operated on, and others, again, were not operated on.

In earlier years, i. e. in the years 1922—1931, 80 severe cases of acute cholecystitis were treated in the hospital. 34 of those were not operated on; 12 among the latter died. 46 were operated on<sup>1)</sup> of which 44 immediately or while the attack was still in progress; in the remaining 2 cases operation was performed in the stage of clinical interval. 16 out of the 46 cases operated on died.

In recent years, i. e. 1932—1935, 59 severe cases of acute cholecystitis were treated. 30 of those were not operated on; among the latter 8 died. 29 were operated on<sup>1)</sup> of which 11 immediately and 5 while the attack was still in progress; the remaining cases were operated on in the stage of clinical interval. 3 died of the 29 cases operated on.

The mortality among the severe cases of acute cholecystitis consequently was lower, even among the cases not operated on, in the later period, in which a smaller number of the cases were operated on, and in which the operations actually performed were to a smaller extent made in the acute stage of the disease.

For the cases not operated on, the mortality was in the early period 35,3 per cent, and in the later period 26,6 per cent. For the cases operated on, the mortality was in the early period 34,8 per cent, and in the later period 10,3 per cent. The difference is statistically probable (diff. =  $24,5 \pm 9,0$ ). Our material gives cause for the assumption that the part of the severe cases of acute cholecystitis which had to be operated on immediately or while the attack was still in progress, is comparatively small (about 1/3 of the cases, if we disregard the hopeless cases which died without being operated on).

The risk of dying after operation for acute cholecystitis is greater for the higher age groups (see table 26). The 3 patients who died

<sup>1)</sup> at first stay in hospital.

after operation for acute cholecystitis in recent years, were 52, 60 and 62 years old.

If the indications for operative treatment of acute cholecystitis employed by us in recent years, were to give an equally low mortality in the future, it will become clear that only a small part of the severe acute cases should be operated on during the acute stage of the disease. We then have the choice of operating on the remaining cases in the stage of interval or of not operating on them. These cases would thus be included among those treated in the following group, that is to say cases with a less severe form of the disease.

In the case of obturating common duct stone we are faced with another situation. Strictly speaking there is no other alternative than operation in order to save the patient. Attempts have been made to remove the common duct stone by duodenal intubation etc., it is true, but these attempts have on the whole been a failure, and we may state that practically all the patients with stone obstructing the passage through the common duct, die from the disease if they are not operated on. The problems which arise in these cases under such circumstances only refer to the suitable treatment prior to the operation, the suitable time at which the operation should be performed, and the suitable after-treatment. These problems, however, fall beyond the scope of the present investigation.

In summing up we may state that in our opinion *the cases which have to be operated on on vital indication are not very numerous. The actually comprise only the most severe cases of acute cholecystitis and the cases with obturating common duct stone.* In our material these cases made up 11,5 per cent, at a high estimate, and 7,4 per cent, at a low estimate, of all cases of gall stone disease. The figures are obtained by relating the number of cases operated on on acute indication during the periods 1922—1931 and 1932—1935 to all the cases treated in these years.

*The medium-severe and mild cases.*

All the remaining cases belong to this group, consequently in our opinion also a large part of the severe cases of acute cholecystitis in which the acute seizure subsided without operation. The cases of common duct stone in which the stone gave mild, or no, clinical symptoms further belong to this group. Finally are referred

to this group the medium-severe and mild cases of cholecystitis and the cases with non-complicated gall stone disease.

Theoretically, we might perhaps treat each of these groups separately. It is however impossible, on the basis of the material available, to obtain sufficiently large groups of cases in order to be able to draw definite conclusions. From a clinical point of view these different cases are fairly similar inasmuch as vital indication for operation is not present. The cases of cholecystitis in which the infection subsides thus may be ranked in the same category with the cases which did not present symptoms of infection. The cases of common duct stone in which the stone owing to its localization did not give obvious clinical symptoms cannot be diagnosed, and the clinical diagnosis in such cases is either non-complicated attack of biliary colic or, in the cases in which the gall bladder is simultaneously inflamed, acute cholecystitis.

The risks to be considered in these mild cases are both the risk of dying and the risk of relapsing. These risks may be weighed against each other and we may ask: is the risk of relapsing, or of dying, from the disease without operation so great that it counterbalances the risk of operation? Each operative interference involves a certain death-risk, by pulmonary embolism, pneumonia, operative injuries, etc.

As regards the risk of relapsing we showed in chapter 5 that this risk is in our material of different magnitude for those who have had at most 2 attacks as compared to those who have had more than 2 attacks. It may consequently be advisable to discuss these two groups of cases separately.

Gall stone patients who have had at most 2 attacks.

Of those who were discharged from the hospital and had not been operated on, 64.6 per cent were clinically healthy and 8.0 per cent had mild symptoms. 27.4 per cent, on the other hand, had severe symptoms, which had either invalidated the patient or later on forced to operation or caused death without operation. Of those who were discharged from the hospital, 72.6 per cent were thus practically healthy. Under the most favourable circumstances we may estimate the risk of operation at between 1 and 2 per cent (the mortality figure obtained in our material for those who were operated on for non-complicated gall stone disease; see table 23). We must,

however, pay regard to the fact that the deaths after operation chiefly occur among elderly patients. The risk figure given accordingly applies to the total material. If we are concerned with elderly patients the risk of operation must be considered to be greater, and in the case of younger patients, it is probably smaller.

The freedom from relapse obtained after operation is in our material greater for those who have had at most 2 attacks than for those who have had several attacks. Among the cases belonging to the former group which were operated on and discharged from the hospital, 95.5 per cent were clinically healthy or had only mild symptoms. If we consequently assume that all the patients who have had at most 2 attacks were operated on, we might theoretically expect to gain a freedom from relapse amounting to about 20 per cent at the expense of an operative mortality of 1 to 2 per cent.

It should be pointed out, however, that the figure for the risk of operation of non-complicated cases must be looked upon as a minimum figure. The material is selected since only such patients are operated on for non-complicated gall stone disease as are considered to have a very good chance of surviving. Aged patients, or such as suffer from another disease or from a reduced general condition, are not readily operated on except on more or less vital indication.

There is still another risk which should be considered in connection with indications for operation, namely the risk of later on dying from the disease. We may obtain an idea of this risk by examining the re-examined material. Of 113 patients on which data were obtained, 2 died from gall stone disease without having been operated on<sup>1</sup>), and 2 died following operation performed for a new attack. The risk of dying from gall stone disease thus is 3.5 per cent for those who were discharged without operation. This risk figure is per se higher than the most favourable figure for the risk of dying after operation. We must pay regard to the fact, however, that those patients who later on died from their disease, with or without operation, were old (one 74 years old, one 72, one 61; only one was younger, 32 years old). Those operated on for gall stone disease also run a risk of subsequently dying from their disease. In our material one patient subsequently died from gall stone disease out of the 66 who had had at most

<sup>1</sup>) Further, one patient died from cancer of the gall bladder.



2 attacks (i. e. 1,5 per cent). The risk of operation among the elderly patients is greater than among those who are younger. Of the non-complicated cases operated on, 3 out of 68 died (i. e. 4,4 per cent), over the age of 50. If the indications for operation were to be widened, we must reckon with the fact that a larger number of elderly patients are also operated on. In chapter 4 we were able to show that the risk of contracting gall stone disease is equally great among older and among younger patients. Under such circumstances there must be found, among the patients who have had at most 2 attacks, a quite considerable number of elderly patients for whom the risk of operation is greater than for the younger patients. We may thus expect that widened indications for operation would result in operation both of a larger number of elderly patients and of a number of patients whose general state of health is not very good.

If we start from the experiences gained on the basis of our material, the situation is as follows for the patients who have had at most 2 attacks. Without operation, about 75 per cent of the discharged patients have no, or slight, discomforts of the disease. The risk of subsequently dying from the disease amounts to about 3 per cent. The operation might be expected to result in 95 per cent of the cases having no, or slight, discomforts of the disease. The risk of an operation in the stage of interval is between 1 and 2 per cent for the total material. For elderly patients the risk of operation is greater. The risk of subsequently dying from gall stone disease is present even for patients operated on.

#### Those who have had more than 2 attacks.

The risk of relapse is much greater for these cases. In our material 34,3 per cent were clinically healthy and 12,3 per cent had mild symptoms. The remaining 53,4 per cent had severe discomforts. Part of the latter had later on been operated on and part of them had died from the disease. The risk of subsequently dying from the disease is of about the same order of magnitude as the one applying to the patients who have had at most 2 attacks. Out of 73 patients, 2 died (i. e. 2,7 per cent), one without being operated on and the other after an operation had subsequently been performed.<sup>1)</sup> After operation, 91,3 per cent of the cases were

<sup>1)</sup> Further, one patient died from cancer of the gall-bladder.

clinically healthy or had only mild discomforts. The risk of dying after operation in the stage of interval is, at best, between 1 and 2 per cent if we count with the mortality figure for operation of non-complicated cases. The patients operated on also run a risk of subsequently dying from gall stone disease. Of the 231 re-examined patients, 1 later died from gall stone disease (i. e. 0,4 per cent).

In summing up we may state that of patients who have had more than 2 attacks, hardly fifty per cent become healthy in the future or have only mild discomforts. If an operation is performed, about 90 per cent have a chance of recovery or of only getting mild symptoms. The risk of operation for the total material may be estimated at between 1 and 2 per cent, if the cases most suited to operation are selected. Elderly patients run a greater risk. Both patients operated on and patients not operated on run a risk of later on dying from gall stone disease.

#### The results of treatment for the total material.

It might be of interest to try to obtain an idea of the result obtained in the treatment of our total clinical material. We start from

Table 46. *All cases, treated in 1922—1930, not operated on during first stay in hospital. Distribution according to results of hospital treatment and of re-examination.*

| Age, years | Number of cases, N |     | Deaths in hospital |        |                 |        | Re-examination     |        |                 |        |                 |                 |                               |                 | Deaths from other disease und-known |    |
|------------|--------------------|-----|--------------------|--------|-----------------|--------|--------------------|--------|-----------------|--------|-----------------|-----------------|-------------------------------|-----------------|-------------------------------------|----|
|            |                    |     |                    |        |                 |        | Clinically healthy |        |                 |        | Mild symptoms   |                 | Severe symptoms <sup>1)</sup> |                 |                                     |    |
|            | M                  |     | W                  |        | M               |        | W                  |        | M               | W      | M               | W               | M                             | W               |                                     |    |
|            | M                  | W   | Number of cases    | % of N | Number of cases | % of N | Number of cases    | % of N | Number of cases | % of N | Number of cases | Number of cases | Number of cases               | Number of cases |                                     |    |
| 0—20       | 1                  | 2   | —                  | —      | —               | —      | —                  | —      | —               | —      | —               | —               | 1                             | 2               | —                                   | —  |
| 20—29      | 5                  | 22  | —                  | —      | —               | —      | 5                  | 100    | 10              | 45     | —               | 2               | —                             | 8               | —                                   | 2  |
| 30—39      | 5                  | 20  | —                  | —      | 1               | 5      | 3                  | 60     | 5               | 25     | —               | 1               | 2                             | 10              | —                                   | 3  |
| 40—49      | 10                 | 29  | —                  | —      | —               | —      | 7                  | 70     | 13              | 45     | —               | 5               | 3                             | 7               | —                                   | 4  |
| 50—59      | 16                 | 33  | 1                  | 6      | —               | —      | 5                  | 31     | 15              | 44     | 3               | 4               | 5                             | 10              | 2                                   | 4  |
| 60—69      | 19                 | 38  | 1                  | 5      | 2               | 5      | 12                 | 63     | 17              | 45     | 1               | 2               | 3                             | 12              | 2                                   | 5  |
| 70—84      | 7                  | 19  | 1                  | 13     | 4               | 18     | 1                  | 13     | 5               | 23     | —               | —               | 3                             | 4               | 2                                   | 6  |
| Total      | 63                 | 163 | 3                  | 5      | 7               | 4      | 33                 | 52     | 65              | 29     | 4               | 14              | 17                            | 53              | 6                                   | 24 |

<sup>1)</sup> inclusive of those later operated on and deaths from gall stone disease.

Table 47. *All cases, treated in 1922—1930, operated on during first stay in hospital. Distribution according to results of hospital treatment and of re-examination.*

| Age, years | Number of cases, N |     | Deaths in hospital |        |                 |        | Re-examination     |        |                 |        |                 |        |                                |        | Deaths from other disease, und unknown |        |
|------------|--------------------|-----|--------------------|--------|-----------------|--------|--------------------|--------|-----------------|--------|-----------------|--------|--------------------------------|--------|----------------------------------------|--------|
|            |                    |     |                    |        |                 |        | Clinically healthy |        |                 |        | Mild symp-toms  |        | Severe symp-toms <sup>1)</sup> |        |                                        |        |
|            | M                  |     | W                  |        | M               |        | W                  |        | M               | W      | M               | W      | M                              | W      |                                        |        |
|            | M                  | W   | Number of cases    | % of N | Number of cases | % of N | Number of cases    | % of N | Number of cases | % of N | Number of cases | % of N | Number of cases                | % of N | Number of cases                        | % of N |
| 0—20       | —                  | 1   | —                  | —      | —               | —      | —                  | —      | 1               | 100    | —               | —      | —                              | —      | —                                      | —      |
| 20—29      | 1                  | 35  | —                  | —      | 1               | 3      | 1                  | 100    | 18              | 51     | —               | 6      | —                              | 3      | —                                      | 7      |
| 30—39      | 8                  | 66  | 1                  | 13     | 1               | 2      | 6                  | 75     | 50              | 76     | 1               | 9      | —                              | 2      | —                                      | 4      |
| 40—49      | 14                 | 72  | 5                  | 36     | 4               | 6      | 7                  | 50     | 46              | 64     | 2               | 12     | —                              | 8      | —                                      | 2      |
| 50—59      | 20                 | 64  | 2                  | 10     | 6               | 9      | 13                 | 65     | 40              | 63     | 2               | 4      | 1                              | 6      | 2                                      | 8      |
| 60—69      | 6                  | 52  | 2                  | 33     | 7               | 13     | 3                  | 50     | 26              | 50     | —               | 5      | 1                              | 4      | —                                      | 10     |
| 70—79      | 3                  | 11  | 2                  | 67     | 3               | 27     | 1                  | 33     | 2               | 18     | —               | —      | —                              | 1      | —                                      | 5      |
| Total      | 52                 | 301 | 12                 | 23     | 22              | 7      | 31                 | 60     | 183             | 61     | 5               | 36     | 2                              | 24     | 2                                      | 36     |

the assumption that every patient was treated in a suitable manner and that, consequently, the interests of the patients who were not operated on, were best served by this and that reasonable indications for operation were adopted in the cases which were operated on. In tables 46—48 the material for the years 1922—1930 is arranged in such a way that, for each age group, is stated the number of cases that died of the disease, during the stay in the hospital, and further the number that after the discharge were clinically healthy, had mild discomforts or severe discomforts. Finally, in the last column, are found the cases which died from another disease or relating to which no data were obtained. We may assume that the state of health among those is probably fairly similar to the one found among the other cases. Percentage figures are given for the deaths and for the clinically healthy cases. The figures are calculated on the basis of the total material, and the tables thus show the number of those who died or recovered out of the patients who came to treatment. In table 46 are found the cases which were not operated on during the first stay in the hospital, in table 47 those who were operated on during the first stay in the hospital, and, finally,

<sup>1)</sup> inclusive of those later operated on and deaths from gall stone disease.

Table 48. *All cases, treated in 1922—1930, operated on and not operated on during first stay in hospital. Distribution according to results of hospital treatment and of re-examination.*

| Age, years | Number of cases, N |        | Deaths in hospital |        |                 |        | Re-examination     |        |                 |        |                 |        |                               |        | Deaths from other diseases and unknown |        |
|------------|--------------------|--------|--------------------|--------|-----------------|--------|--------------------|--------|-----------------|--------|-----------------|--------|-------------------------------|--------|----------------------------------------|--------|
|            |                    |        |                    |        |                 |        | Clinically healthy |        |                 |        | Mild symptoms   |        | Severe symptoms <sup>1)</sup> |        |                                        |        |
|            | M W                |        | M W                |        | M W             |        | M W                |        | M W             |        | M W             |        | M W                           |        |                                        |        |
|            |                    |        |                    |        |                 |        |                    |        |                 |        |                 |        |                               |        |                                        |        |
|            | Number of cases    | % of N | Number of cases    | % of N | Number of cases | % of N | Number of cases    | % of N | Number of cases | % of N | Number of cases | % of N | Number of cases               | % of N | Number of cases                        | % of N |
| 0—20       | 1                  | 3      | —                  | —      | —               | —      | —                  | —      | 1               | 33     | —               | —      | 1                             | 2      | —                                      | —      |
| 20—29      | 6                  | 57     | —                  | —      | 1               | 2      | 6                  | 100    | 28              | 49     | —               | 8      | —                             | 11     | —                                      | 9      |
| 30—39      | 13                 | 86     | 1                  | 8      | 2               | 2      | 9                  | 69     | 55              | 64     | 1               | 10     | 2                             | 12     | —                                      | 7      |
| 40—49      | 24                 | 101    | 5                  | 21     | 4               | 4      | 14                 | 58     | 59              | 58     | 2               | 17     | 3                             | 15     | —                                      | 6      |
| 50—59      | 36                 | 97     | 3                  | 8      | 6               | 6      | 18                 | 50     | 55              | 56     | 5               | 8      | 6                             | 16     | 4                                      | 12     |
| 60—69      | 25                 | 90     | 3                  | 12     | 9               | 10     | 15                 | 60     | 43              | 48     | 1               | 7      | 4                             | 16     | 2                                      | 15     |
| 70—84      | 10                 | 30     | 3                  | 27     | 7               | 21     | 2                  | 18     | 7               | 21     | —               | —      | 3                             | 5      | 2                                      | 11     |
| Total      | 115                | 464    | 15                 | 13     | 29              | 6      | 64                 | 55     | 248             | 53     | 9               | 50     | 19                            | 77     | 8                                      | 60     |

in table 48 the total material. As regards the cases not operated on table 46 shows that 43,4 per cent (98 out of 226) have been healthy and that 18 have had mild symptoms. The chances of recovery, or of being relatively recovered, are about equally great for the different age classes. The risk of dying principally reveals itself among the higher age groups of the cases not operated on. Of the 10 patients who died, 9 were over the age of 50. As regards the cases operated on table 47 shows that 214 out of 353 were clinically healthy (i. e. 60,6 per cent) and 41 had mild symptoms. In all 255 patients were practically healthy. The percentage of deaths is greater among the cases operated on than among the cases not operated on. 34 out of 353 died (i. e. 9,6 per cent) whereas 10 out of 226 cases died among those not operated on (i. e. 4,4 per cent). The relatively high mortality among the patients operated on should largely be explained by the fact that the mortality among the cases of acute cholecystitis was relatively high during the earlier years. If we calculate the mortality after operation among those who were operated on during the years 1932—1935, we find that 8 died out of 180 (i. e. 4,4 per cent). In these years in

<sup>1)</sup> inclusive of those later operated on and deaths from gall stone disease.



which, to a larger extent than previously, operation was avoided in the acute stage, the mortality thus decreased, reaching the same order of magnitude as the one relating to the patients not operated on. Table 48 shows that of the total material of treated patients 53,9 per cent (312 out of 579) were healthy and 59 had mild symptoms. In all 371 patients were practically healthy, i. e. 64 per cent of the 579 treated patients. 44 out of 579 died (i. e. 7,6 per cent).

The patients not operated on are partly such cases as had mild attacks and on this account were not operated on, and partly such patients as had more severe attacks but who were not operated on owing to advanced age, other disease, etc., and partly patients who belonged to the group of the most severe cases and who died without operation. It might be assumed that the mortality among the cases not operated on is the mortality that applies to gall stone disease per se. If the mortality among the cases operated on is higher than among the cases not operated on, the difference in mortality would be an expression of the death-risk incurred in order to obtain the smaller risk of relapse resulting from operation.

In summing up we may maintain that our material does not support the view that widened indications for operation would bring about a more favourable situation for the patients with regard to the risk of dying. It is naturally difficult to obtain exact information on this point but this much we should be justified in stating: as only a small number of patients, that is to say only part of those who have had severe acute cholecystitis, and those who present obstruction of the common duct, have to be operated on on vital indication, and as, further, the risk of subsequently dying from the disease is about equally great among those who are operated on and among those who are not operated on, the post-operative mortality for the non-complicated cases is an expression of the lowest price we have to pay in order to obtain a lessened risk of relapse. If the indications for operation in non-complicated cases are widened, and especially if a larger number of elderly patients are operated on, we may reckon with the fact that the risk of dying after operation increases. Simultaneously, we obtain a smaller risk of relapse among the patients operated on.

In the above discussion we have chiefly dealt with the risk of dying and the risk of becoming invalidated by the disease.

Now the fact is that many patients who have comparatively harmless attacks are much troubled by the often very painful seizures and in consequence willingly subject themselves to an operation in order to get rid of them, even with a knowledge of the risk involved in an operation. What we have wanted to analyse above is the risks if we operate, or if we do not operate. We have further wanted to point out that there exists a risk of the mortality of gall stone disease increasing if the indications for operation are widened. Theoretically speaking, the best plan would naturally be to operate in the stage of interval if we are forced to an operation. We have shown that, in view of the risk of dying, we need only operate on a minor part of the severe cases in the acute stage. Theoretically, it might be imagined that we only were to operate under two circumstances: on one hand, part of the severe acute cases have to be operated on in the acute stage as also the cases with common duct obstruction. On the other hand, we might in the other cases try to operate only during the stage of interval. In the case of acute cholecystitis, the inflammatory symptoms in the gall bladder subside only after a comparatively long time. It has therefore been emphasized in many quarters that operation ought to be performed a comparatively short time after the acute attack. It has been pointed out that the patient is in most cases inclined to operation relative to the acute attack, but that a patient who has been discharged from a hospital after the attack has passed, is extremely reluctant to return in a free interval in order to submit himself to an operation which after all involves a certain death-risk. This would mean that a greater importance is ascribed to the patient's judgment while the attack is in progress, than the maybe unpremeditated view he expresses after the attack has once subsided. In the last resort it is up to the patient to decide whether an operation is to be performed or not. But the patient naturally may be entitled to the clearest possible exposé of the situation in order to form an opinion.<sup>1)</sup>

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<sup>1)</sup> 68 patients refused the proposed operation. None of these died during the stay in the hospital. 36 were re-examined. Of these 14 were healthy, 7 had mild symptoms and 4 had severe symptoms. Finally, 11 out of the 36 patients had subsequently been operated on for gall stone disease.

Finally it must be pointed out that the survey given in a preceding chapter (chap. 4) of the gall stone disease from the point of view of the population means that the risk of contracting gall stone disease is present in all age groups and that, for the more advanced ages, it shows rather a tendency to increase than to decrease. This means in its turn that the view held in many quarters to the effect that gall stone disease is a disease having its maximum in middle life, is not correct. If elderly people run a risk of contracting gall stone disease which is at least as great as the one incurred by younger people, it follows that in a clinical material we might expect to find a relatively large number of elderly persons who have recently been taken ill. As, further, the risk of relapse in an early stage of the disease is comparatively small, even if no operation is performed, we should naturally try to avoid operation, if possible, in such cases. The risk of dying is considerably greater for older patients than for younger. Our material shows, as appears in table 14, that the risk of dying is in elderly people greatest during the year immediately following the first attack (for younger people it is the other way round). If, consequently, in the case of an elderly patient, we may cause the acute attack to subside, we have less reason to operate, since, for one thing, the risk of relapse is small and, also, the risk of subsequently dying from the disease is comparatively small. The latter naturally to a certain extent is related to the fact that the remaining duration of life is comparatively short for elderly people.

## Summary.

The material on which the present investigation is based is made up of diary material from the Academical Hospital, autopsy material from the Pathological Institution in Uppsala, and data on deaths obtained from the Central Statistical Bureau of Sweden.

After a review of the literature, especially relating to the treatment and prognosis of the gall stone disease the author tried to analyse the risk factors in this disease.

1. In the first place a calculation was made of the risk of developing gall stone incurred by men and women at different ages. The risk increases at first rapidly and then keeps fairly constant up to an advanced age. The risk appears about the age of 30 in men and about the age of 20 in women. It increases somewhat with age but keeps fairly constant for men at 200 cases per 100 000 inhabitants and for women at about 400 cases per 100 000 inhabitants.

The risk of being taken ill is smaller as all those who have gall stone do not develop symptoms of gall stone disease. It increases rapidly in early years and, after the age of 40 in men and the age of 30 in women, it keeps fairly constant at between 50 and 100 cases per 100 000 inhabitants for men and between 100 and 200 cases per 100 000 inhabitants for women. The risk of contracting the disease is about double for a woman as compared to a man at the corresponding age.

Finally, the death-risk was calculated. It increases in men from the age of 40 towards more advanced ages and in women from the age of 30 towards more advanced ages. At the age of 60 it attains a value of between 25 and 50 deaths per 100 000 inhabitants among men; among women the corresponding figures are somewhat higher. For details, the reader is referred to figs. 3 and 4 and to chapter 4.

On the basis of the above-mentioned risk figures, the risk of developing symptoms of disease was calculated for a person with gall stone. For men with stones, the risk of falling ill keeps roughly at between 20 and 40 per cent and for women we obtain corresponding figures, which means that more than half of the cases of gall stone



have no morbid symptoms. The risk of dying for a person falling ill keeps at about 3—6 per cent among younger people but rises towards more advanced ages up to 20—30 per cent. We are here concerned with approximate figures which only aim at giving a rough survey of the situation.

In the subsequent discussion the author tried to give a more detailed statistical analysis of the risk factors involved in the cases of disease.

2. In order to obtain a more differentiated picture of the risks applying to the diseased persons, an investigation was made into the mortality and the risk of developing symptoms during the subsequent course of life, both for the cases operated on and for the cases not operated on. During the period 1922—1935, 498 patients were treated who had *not been operated on* during the first stay in the hospital. This group is divided into patients with symptoms only of cholelithiasis and patients with cholecystitis. The former group comprises 189 cases, with no death. The latter group comprises 309 cases with a mortality of 6,5 per cent. The deaths are discussed in detail with regard to indications and contra-indications for operation. This examination shows that, in 18 cases, we must, on the basis of our present knowledge, consider that no operation ought to have been performed, and that, only in two cases, it might be debateable whether the patient could have been saved by an operation. This is only a possibility, however, and on the whole the contra-indications adopted appear to be justified.

3. As it is of particular interest to obtain an idea of the risk of relapse for the cases not operated on and as the data given in the literature on this point are not very elucidative, a re-examination was made of patients who had been treated during the period 1922—1930. The time of observation was 6—9 years. Only in a few cases, it was shorter than 5 years. Of the 226 patients discharged from the hospital, no information could be obtained on 7. Further, 28 patients had died, 3 among those from gall stone disease and 2 from cancer of the gall bladder. As regards relapses, it is shown that 76 per cent of the relapses occur within the first 3 years of the discharge from the hospital and 90 per cent within 5 years. In order to obtain complete data it is consequently imperative that the time of observation should not be less than 5 years. As regards the risk of relapse, we find that those who have had at most 2 attacks run

a smaller risk of relapse than those who have had several attacks at the time of the first treatment. Among those who had had 2 attacks at most, 65 per cent were clinically healthy, 8 per cent had mild discomforts and 27 per cent severe discomforts (among the latter 3 cases had died and 21 cases had later been operated on). Among those who had had more than 2 attack 34 per cent were healthy, 12 per cent had mild symptoms and 53 per cent had severe symptoms (inclusive of 26 cases which had subsequently been operated on and 2 cases which had died). Among those who had had more than 2 attacks, no difference could be found as regards risk of relapse between those who had had attacks during a short time and those who had had attacks over a more prolonged period. No difference in the risk of relapse could be found, either, between those who had had a non-complicated form of the disease and those who had acute cholecystitis.

4. An examination of the cases *operated on* yielded the following result. The material, which refers to the years 1932—1935, comprises 620 cases. 57 out of these had previously been treated in the clinic but had not been operated on on that occasion. The post-operative mortality was first examined.

Among non-complicated cases, 261 in number, 5 cases died following operation, of which 3 from pulmonary embolism. If we distinguish between cases of cholelithiasis without inflammation and cases of chronic cholecystitis, we find that the former group comprises 175 cases with one death, and the latter group 86 cases with 6 deaths. The difference might well be due to chance.

5. The material of acute cholecystitis comprises 257 cases. As regards this group, divergent views are held as to the suitable time at which operation should be performed. The question is whether operation should be performed early during the attack or later when the attack has more or less subsided. During the years 1922—31 a comparatively great percentage of the cases were operated on in an early stage. Of 171 cases operated on, 24 died, i. e. 14 per cent. In the subsequent period, 1932—35, in which operation was preferably performed in the *free interval*, 86 cases were operated on. Of these, 3 died, i. e. 3.5 per cent. The difference in mortality is statistically significant. Naturally, it cannot simply be asserted that this difference is related to modified indications for operation. The material might have changed in character. In view of this possibility we

examined whether a displacement in age had occurred in the material. No such displacement could be demonstrated. It was not possible to show, either, that the cases were different in regard to the frequency of the more or less severe grades of the disease. About the same percentage of the patients admitted were operated on in the different periods. The mortality among the cases not operated on was of about the same order of magnitude in both periods. No change was found in the technique of operation, the methods of anaesthesia, etc. which might explain the difference. Under such circumstances the most probable explanation of the decreased mortality is that the operations were to a larger extent performed after the attack had more or less subsided, that is to say when the acute symptoms had improved, the temperature decreased and the patient might be allowed out of bed. This explanation naturally is not proved to be correct as unknown factors might have exerted their influence. In all operation statistics and in every evaluation of the results of operations we must reckon with the possibility that materials which seem to be comparable may present differences which have escaped our notice. The author makes comparisons on this point with some other materials in order further to illustrate the situation. As regards the severe cases of acute cholecystitis which have to be operated on in the acute stage, it is pointed out that this group is small and that the death-risk run by those patients is a high one. It seems reasonable that they should be treated by the least complicated operation possible, that is to say cholecystostomy.

6. The author's material comprises 102 cases of common duct stone which were operated on. 14 of these died at the operation. The author tried to analyse the material as to the nature of the symptoms, that is to say whether the common duct stone had given clinical symptoms or not, and whether fever had been present or not. In view of the fact that the material is small, conclusions can only be drawn to a limited extent. The mortality, however, is relatively high for clear cases of common duct obstruction, and considerably lower for cases which gave no, or doubtful, symptoms of common duct stone.

7. In order to orientate on the risk of subsequently getting symptoms among the cases operated on, a re-examination was made of those who were operated on in the period 1922—30. The material comprises 348 cases, among which no information was obtainable

on 15 cases. In the case of 7 cases no information was given as to the time during which they were ill before they were operated on. Further, 31 patients had died, 2 among those from gall stone disease. If these 2 cases are included, we find that, among 297 cases, 78 per cent were clinically healthy, 14,2 per cent had mild discomforts, and 7,8 per cent had severe discomforts. In the last-mentioned group, which comprises 23 cases, 10 had subsequently been operated on and 2 had died. The material was further divided into cases with at most 2 attacks and cases with several attacks. In the former group, 87,9 per cent were healthy, in the latter group, 75,3 per cent. (The difference is statistically probable.) For the cases who had had more than 2 attacks, no difference in risk could be shown between those who had had attacks during a short time and those who had had attacks over a more prolonged period. Neither could any difference be found between younger and older patients, or between men and women.

8. The material further was divided according to various forms of the disease. Among non-complicated cases, 78,5 per cent were clinically healthy of 135 cases; among those who had had at most 2 attacks, 94,4 per cent were clinically healthy, and among those who had had more than 2 attacks, 76,1 per cent were clinically healthy. The difference is statistically probable. Among non-complicated cases, 76,5 per cent were clinically healthy of 85 cases without inflammatory symptoms. Among those who had at most 2 attacks, a greater percentage was clinically healthy than among those who had had more than 2 attacks. Of 50 patients among non-complicated cases presenting chronic cholecystitis, 82 per cent were clinically healthy.

Among cases of acute cholecystitis, 80,7 per cent were clinically healthy in a material of 114 cases. Those who had had at most 2 attacks were healthy in a greater percentage of cases than those who had had more than 2 attacks.

Among 48 patients with common duct stone, 34 per cent were clinically healthy. The author gives an account of 9 cases on which cholecystectomy was performed in 8 cases and cholecystectomy + choledocholithotomy in 1 case and which were later re-operated on owing to suspicion of common duct stone: stone was found in 6 of these cases.

9. In order to obtain a general picture of the prognosis with



regard to the possibilities of treatment, the author discusses the two alternatives: operation or no operation. In the first place it is shown that the intervals between the beginning of the disease and the operation are equally long in complicated cases of gall stone disease and in non-complicated cases, whereas the average age at which the disease appears is higher in the complicated cases than in the non-complicated cases. This indicates that the risk of contracting a complicated form of the disease is greater at a more advanced age whereas, on the other hand, the duration of the disease is not of equally decisive importance.

10. In forming an idea of the risk factors generally we must distinguish between severe cases and less severe cases. In severe cases an imminent death-risk is present and special reasons for operating may be present in order to prevent a fatal issue.

The author points out that, in so far as we may judge from the Uppsala material, we have reason to assume that operation had to be performed only in a rather small percentage of the cases; the figures rather indicate that a certain abstention from operation yields a lower mortality than a more active line of treatment. For details, the reader is referred to chapter 6. The largest part of the material comprises cases in which operation owing to an impending death-risk was not considered necessary. If we first look at the group of cases which had had at most 2 attacks, we find that an operation implies a death-risk which may be estimated at 1—2 per cent under the most favourable conditions. If we operate, however, we lessen the risk of relapse from 25 per cent to 5 per cent. The line of action to be adopted naturally depends on the nature of the case and the personal attitude held by the patient in regard to death-risk and risk of relapse and subsequent discomforts.

11. Among patients who have had more than 2 attacks, we may count with a risk of operation of 1—2 per cent under the most favourable conditions being somewhat greater for older than for younger patients. The risk of relapse is in this group greater; the gain may be roughly estimated at 40 per cent of cases which by operation escape from symptoms but had otherwise probably developed symptoms.

As the problems in this field are extremely varying in character, the reader is referred particularly to chapter 6 for details but also to other chapters.

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